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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS			
(57) Abstract			
<p>The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.</p>			

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## DESCRIPTION

Human Proteins Having Hydrophobic  
Domains and DNAs Encoding These Proteins

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TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

20

BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip, so that there are

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hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is expected to lead to development of novel pharmaceuticals utilizing these proteins.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto-cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,



the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

#### OBJECTS OF THE INVENTION

The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

#### BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

- Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.
- Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.
- Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.
- Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.
- Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.
- Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.
- Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.
- Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.
- Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.
- Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.
- Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.
- Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.
- Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.
- Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.
- Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.
- Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10563.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01467.

5 Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01956.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02545.

10 Fig. 24 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02551.

Fig. 25 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 26 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02632.

15 Fig. 27 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10488.

Fig. 28 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10538.

20 Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10542.

Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10571.

Fig. 31 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01470.

25 Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02419.

Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

30 Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02695.

Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10031.

SUMMARY OF THE INVENTION

- Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.
- Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.
- Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.
- Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.
- Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10592.
- Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10593.
- Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10594.
- Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10595.
- Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10596.
- Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10597.
- Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10598.
- Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10599.
- Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10600.
- Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10601.
- Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10602.

As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention.

5 In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides cDNAs coding

10 for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in

15 eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

#### DETAILED DESCRIPTION OF THE INVENTION

20 The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the

25 hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of

30 the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T7, T3, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

In the case where one of the proteins of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region.

5 Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the

10 pET expression system, the pGEX expression system, and so on.

In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-

15 membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pKAl,

20 pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells,

25 *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium

30 phosphate method, the liposome method, the DEAE-dextran method, and so on.

After one of the proteins of the present invention is

expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic chromatography, affinity chromatography, reverse phase chromatography, and so on.

The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the



scope of the present invention.

The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method  
5 by cDNA cloning, and so on.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)<sup>+</sup> RNAs extracted from human cells. The human cells may be  
10 cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and  
15 Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can  
20 be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according  
25 to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as  
30 the primers for the RT-PCR method using an mRNA isolated from human cells.

The cDNAs of the present invention are characterized by

comprising either of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA was obtained, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saas-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10568	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saas-2	937	229
33, 43, 53	HP02575	Saas-2	1678	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saas-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saas-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saas-2	1753	327
64, 74, 84	HP02551	Saas-2	1117	223
65, 75, 85	HP02631	Saas-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saas-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Sa0s-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Sa0s-2	2168	487
96, 106, 116	HP10530	Sa0s-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02798	HT-1080	1136	267
124, 134, 144	HP10041	Sa0s-2	619	106
125, 135, 145	HP10246	XB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Sa0s-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and

131 to 150 shall come within the scope of the present invention.

In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

#### Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be

administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganisms is cultured.

#### Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaB3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, W1165, HT2, CTL2, TF-1, M07e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

25 Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Colligan, A.M. Krusisbeeck, D.H. Margulies, E.M. Shevach, W Strobeck, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnoli et al., J. Immunol. 145:1706-1712, 1990; Bertagnoli et al., Cellular



Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

- Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon  $\gamma$ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

- Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 - Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.

6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

**Immune Stimulating or Suppressing Activity**

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as affecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, leishmania spp., malaria spp.

and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

5        Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune  
10        thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly  
15        allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

      Using the proteins of the invention it may also be  
20        possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by  
25        suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing  
30        non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockade of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or

tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., *Science* 257:789-792 (1992) and Turka et al., *Proc. Natl. Acad. Sci. USA*, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., *Fundamental Immunology*, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

- autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythematosus in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul et al., *Fundamental Immunology*, Raven Press, New York, 1989, pp. 840-856).
- 10 Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.
- 20 Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the
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- 30

transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and , microglobulin protein or an MHC class





Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses  
5 and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In  
10 vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly  
15 Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse  
20 Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify,  
25 among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079,  
30 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,

1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhargava et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

5 Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zama et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

15 Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad. Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

25 A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylnitrosourea colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 265-268, Wiley-Liss, Inc., New York, NY, 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; primitive hematopoietic colony forming cells with high proliferative potential, McNeice, I.K. and Bridgell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 23-39, Wiley-Liss, Inc., New York, NY, 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Plomacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 1-21, Wiley-Liss, Inc., New York, NY, 1994; Long term marrow cultures in the presence of stromal cells, Spooner, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 163-179, Wiley-Liss, Inc., New York, NY, 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol. pp. 139-162, Wiley-Liss, Inc., New York, NY, 1994.

# Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is

not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of central nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

5 Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

10 It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including  
15 vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

20 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

25 A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

30 Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491

(skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound

Healing, pps. 71-112 (Mabach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglestein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

# Activin/Inhibin Activity

10 A protein of the present invention may also exhibit

activin- or inhibin-related activities. Inhibins are

characterized by their ability to inhibit the release of

follicle stimulating hormone (FSH), while activins and are

characterized by their ability to stimulate the release of

15 follicle stimulating hormone (FSH). Thus, a protein of the

present invention, alone or in heterodimers with a member of

the inhibin family, may be useful as a contraceptive based

on the ability of inhibins to decrease fertility in female

mammals and decrease spermatogenesis in male mammals.

20 Administration of sufficient amounts of other inhibins can

induce infertility in these mammals. Alternatively, the

protein of the invention, as a homodimer or as a heterodimer

with other protein subunits of the inhibin- group, may be

25 useful as a fertility inducing therapeutic, based upon the

ability of activin molecules in stimulating FSH release from

cells of the anterior pituitary. See, for example, United

States patent 4,798,885. A protein of the invention may

also be useful for advancement of the onset of fertility in

sexually immature mammals, so as to increase the lifetime

30 reproductive performance of domestic animals such as cows,

sheep and pigs.

The activity of a protein of the invention may, among



other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; 5 Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

#### Chemotactic/Chemokinetic Activity

10 A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a 15 desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or 20 neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or 25 indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing 30 such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Krusbeek, D.H. Margulies, R.M. Shevach, W. Strobeck, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APWIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

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without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

#### Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

5 Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Blier et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltzenberg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

#### Anti-inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

#### Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A

protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

10       Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

Examples

The present invention is specifically illustrated in more detail by the following examples, but examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saso-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA libraries. Full-length cDNA clones were selected from  
5        respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for  
10        the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region  
15        being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

#### (2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present  
20        invention was used for in vitro transcription/translation with a T<sub>8</sub>T rabbit reticulocyte lysate kit (Promega). In this case, [<sup>35</sup>S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit.  
25        Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l  $\mu$  of T<sub>8</sub>T rabbit reticulocyte lysate, 0.5  $\mu$ l of a buffer solution (attached to the kit), 2  $\mu$ l of an amino acid mixture (without  
30        methionine), 2  $\mu$ l of [<sup>35</sup>S]methionine (Amersham) (0.37 MBq/ $\mu$ l), 0.5  $\mu$ l of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

out by adding to this reaction system 2.5  $\mu$ l of a canine pancreas microsomal fraction (Promega). To 3  $\mu$ l of the SDS resulting reaction solution was added 2  $\mu$ l of the sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

(3) Expression by COS7

*Escherichia coli* cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2XYT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13KO7 (50  $\mu$ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TB). The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc), well diameter: 3 cm) were inoculated with  $1 \times 10^6$  COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDEM). To the resulting cells was added a suspension of 1  $\mu$ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3  $\mu$ l of



TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the culture medium was replaced by a culture medium containing [<sup>35</sup>S]cystine or [<sup>35</sup>S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

#### (4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (GenBank Accession No. Z93382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

5 elegans hypothetical protein F45G2.c (CE). Therein, the marks of '-', '\*' and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region.

Table 2

10	HP	MAKYLIAQIIVWGVGVCFAPVALRQEF-----AASRAAADAPAGRAGHRSAASNLIS- * * * * * * * * * *
	CE	MPWRTALIKVALAAGEAVAKALTTRAVRDEIRKQTQQAARHAASFTGQASFTRENNASNAKL * * * * * * * * * *
15	HP	GLSLQIAQOQIILNV-SKLSPREEVQKNVNEHLFKVNDKDSVGVGSFYLGSKVVFRAKERLDEEL-K * * * * * * * * * *
	CE	GISLEESLTQILNVKTPILNREEVREKHKVYEHLFNFNINDKSKKGGLTYLGSKVVFRAKERIDEEFGF * * * * * * * * * *
	HP	IQAQDEREKQGMPHY
	CE	ITLKEKKKKKEENAKTE

20 Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. AA338859) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30 <HP02593> (SEQ ID Nos. 2, 12, and 22)  
Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,



Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA306490) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10195> (SRQ ID Nos. 3, 13, and 23)

Determination of the whole base sequence of the cDNA insert of clone HP10195 obtained from cDNA library of human fibrosarcoma HT-1080 revealed the structure consisting of a 286-bp 5'-untranslated region, a 729-bp ORF, and a 604-bp 3'-untranslated region. The ORF codes for a protein consisting of 242 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was somewhat larger than the molecular weight of 27,300 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed the registration of sequences that were similar to the Aplysia VAP-33 (SWISS-PROT Accession No. P53173). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the Aplysia VAP-33 (AP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the



determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in  
5 COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for  
10 example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

15 <HP10507> (SEQ ID Nos. 6, 16, and 26)

Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-  
20 untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
25 Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

Furthermore, the search of the GenBank using the base  
30 sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. A143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10566> (SEQ ID Nos. 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the



hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,452 predicted from the ORF. When expressed in COS7 cells, an expression product of about 12 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W79821) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10567> (SEQ ID Nos. 9, 19, and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10567 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 77-bp 5'-untranslated region, a 375-bp ORF, and a 133-bp 3'-untranslated region. The ORF codes for a protein consisting of 124 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 14,484 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA428475) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

30 The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen



of sequences that shared a homology of 90% or more (for example, accession No. T24595) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01426> (SEQ ID Nos. 31, 41, and 51)

determination of the whole base sequence of the cDNA insert of clone HP01426 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 1-bp

5'-untranslated region, a 942-bp ORF, and a 122-bp 3'-untranslated region. The ORF codes for a protein consisting of 313 amino acid residues and there existed a putative secretory signal. Figure 11 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 34,955 predicted from the ORF. In this case, the

addition of a microsomal led to the formation of a product of 38 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exists in the

amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ser-Ser at position 163). Application of the (-3,-1) rule, a method for predicting the

cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from tryptophan at position 17. When expressed in COS7 cells, an expression product of about 39 kDa was observed in the supernatant

fraction and the membrane fraction. The search of the protein data base using the amino acid sequence of the present protein revealed that the



Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. R06009) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02515> (SEQ ID Nos. 32, 42, and 52)

Determination of the whole base sequence of the cDNA insert of clone HP02515 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 176-bp 5'-untranslated region, a 690-bp ORF, and a 71-bp 3'-untranslated region. The ORF codes for a protein consisting of 229 amino acid residues and there existed a putative secretory signal at N-terminus and one putative transmembrane domain at the C-terminus. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was almost identical with the molecular weight of 26,000 predicted from the ORF. In this case, the addition of a microsomal fraction to the formation of product of 25.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from phenylalanine at position 28.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human T1/ST2 receptor binding protein (Genbank Accession No. U41804). Table 7 shows the

comparison between amino acid sequences of the human protein of the present invention (HP) and the human T1/ST2 receptor binding protein (T1). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 55.8% in the entire region.

10

Table 7

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15 HP  MGDKIWLFFPVLLLAALFPVLLPGAAGTFPSLSDSFTFLPAGQKCEFYQPMFLKASLE
      * . . . . * . . . . * . . . . * . . . . . . . . . . * . . . . .
      TI  MMAAGAALALALWL--MPPVEV--GGAGPPPIQDGEFTFLPAGRKQCFYQSAFANASLE
20 HP  IEYQVLQDAGGLIDIFHLASPEGKTLVFEQRKSDGVHVTVE--TEVDYMFCDNTFTSTISEK
      ***** . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
      TI  IEYQVVGAGGLDVDTFLESPGVGLLVSESRAKDGVHVTVEPTAGDYKLCFDSNFSTISEK
      HP  VIFFELILDNMGEQAQEDEDWKYYITGTDLDMKLEIDILESINSIKSRLSKSGHIQILLR
      . . . . . * . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
20 TI  LVFFELIFDSI--QDDEEVGEWAEAVEPEMLDVKMKEDIKESIETMRTRLESIQMLTLRL
      HP  AFEARDRNIQESNFDVRNFWSMVNLVVMVVVSAIQVYMLKSLFEDKRKRST
      ***** . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
      TI  AFEARDRNIOEGLERNVFNWSAVNVAVLVLLVAVLOVCTLRKFODKRPVPT

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA381943) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

determination of the whole base sequence of the cDNA insert of clone HP02575 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1404-bp ORF, and a 219-bp 3'-untranslated region. The ORF codes for a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 13 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was almost identical with the molecular weight of 54,065 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 57 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exist in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Arg-Thr at position 171, Asn-Ser-Thr at position 239 and Asn-Asp-Thr at position 377). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 29. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human  $\alpha$ -L-fucosidase (SMISS-PROT Accession No. P04066). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human  $\alpha$ -L-fucosidase (FC). Therein,



the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both  
 5 proteins shared a homology of 54.8% in the entire region.

Table 8

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	HP	MRPQELPRLAFPLLLLLLLLLLPPPC-PAHSATRFDPWESLDARQLPAWFDQAKFGIFI
10		***** * . . . . . * . . . * . . . * . . . * . . . * . . . *
	FC	MRSRPAGPALLLLLLFLGAESVRRQPPRRYTPDWPSLDSRPLPAWFDQAKFGVFI
	HP	HWGVSFVPSEFGSEFWWYQKEKIPKIVEFMKDNYPSPFKYEDFGPLFTAKFFNANQWAD
		***** . . . . . * . . . * . . . * . . . * . . . * . . . *
	FC	HWGVSFVPWGWSEFWWWHQEGRPQYQRFMRDNYPPGFSYADFGPQFTARFFHPEEWAD
15	HP	IFQASGAKYIVLTSKHHEGFTLWGSEYSWNWNAIDEGPKRDIVKELEVAIRNRDRLRFGI
		***** . . . . . * . . . * . . . * . . . * . . . * . . . *
	FC	LFQAGAKYVVLTKKHHEGFTNWSPSVSWNWSKDVGPHRDLVGELGTALRKR-NIRYGL
	HP	YYSLFWFHPLFLEDESSFFHKRQFPVSKTLPELYELVNNYQPEVLWSDGDGGAQDPQYWN
		***** * . . . . . * . . . * . . . * . . . * . . . * . . . *
20	FC	YHSLEWFHPLYLLDKNGFKTQHFVSAKTMPELYDLVNSYKPDLIWSDGEWECPTIYWN
	HP	STGFLAWLYNESPVRGTVTVNDRWGAGSICKHGGFYTCSDRYNPGHLLPHKWENCMTIDK
		***** . . . . . * . . . * . . . * . . . * . . . * . . . *
	FC	STNFLSWLYNDSPVKDEVVNVDRWGQNCSCHHGGYNCEDKFKPQSLPDHKWEMCTSIDK
	HP	LSWGYRREAGISDYLTIELVKQLVETVSCGNLLMNIGPTLDGTISVVFEERLRQMGSW
25		***** . . . . . * . . . * . . . * . . . * . . . * . . . *
	FC	FSWGYRRDMALSDVTESEIISLVQTVSLGNYLLNIGPTKDLGIVPIFQERLLAVGKW
	HP	LKVNGEAIYETHTWRSQNDTVTPDVWYTSKPKKLVYAIPLKWPTSGQLFLGHPKAILGA
		***** . . . . . * . . . * . . . * . . . * . . . * . . . *
	FC	LSINGEAIYASKPVRVQWEKNTTSVWYTSKGS--VYAIFLHWPEGVNLESPIIT-ST
30	HP	TEVKLLGHGQPLNWISLEQNGIMVELPQLTIHQPCWKGWALALTNVI
		***** * . . . . . * . . . * . . . * . . . * . . . * . . . *
	FC	TKITMLGIQGLDKWSTDPDKGLFISLPQLPPSAVPAEFAWTIKLTGVK

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<HP10447> (SEQ ID Nos. 35, 45, and 55)  
Determination of the whole base sequence of the cDNA

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. AA477156) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

Determination of the whole base sequence of the cDNA insert of clone HP10357 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 113-bp 5'-untranslated region, a 300-bp ORF, and a 54-bp 3'-untranslated region. The ORF codes for a protein consisting of 99 amino acid residues and there existed two putative transmembrane domains. Figure 14 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 11 kDa that was almost identical with the molecular weight of 10,923 predicted from the ORF.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. N28668) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

insert of clone HP10447 obtained from cDNA library of human liver revealed the structure consisting of a 271-bp 5'-untranslated region, a 570-bp ORF, and a 34-bp 3'-untranslated region. The ORF codes for a protein consisting of 189 amino acid residues and there existed five putative transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA296976) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10477> (SEQ ID Nos. 36, 46, and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10477 obtained from cDNA library of human liver revealed the structure consisting of a 149-bp 5'-untranslated region, a 1092-bp ORF, and a 15-bp 3'-untranslated region. The ORF codes for a protein consisting of 363 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,884 predicted from the ORF.

The search of the protein data base using the amino



of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10513> (SEQ ID Nos. 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10513 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 134-bp 5'-untranslated region, a 750-bp ORF, and a 0-bp 3'-untranslated region. The ORF codes for a protein consisting of 249 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 27,373 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0512 (GenBank Accession No. AB011084). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0512 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 31.6% in the C-terminal region of 196 amino acid residues.

Table 10

HP MGPRGAGWVAAGLLTGAGACVCIPTLTGRBRG

KI KGRGRPRVAMQGRKPRFPFYDEILIGVRDLRKVIALTLQKSDPFIQGVALLTLNNANYSCN  
HP DREGIRGSSKSAEDLTDGSDYDVVLNABEQTLTYLTLESJEDPVIIRALITLGNNAATSV

KI QETIRKLGGLPIIANNINIKTPPHIKKAKALMAMNNLTSENENQGRLOVMNKVMDIMASN

HP NQAIIRKLGGLPIIANNINIKTPPHIKKAKALMAMNNLTSENENQGRLOVMNKVMDIMASN

KI INSAVQVVGTLKFLITNMTITNDYOHILVNSIANF--FRLTSGGGGKIKVRIKILSNFAEN

HP PAMTEGILTRAQVDBSSFLSYDSHVAKEIILTLVTLQNKIKNCIKIIGHIALAVQPTFGSL

KI PDMKKLTLSTQVPASFSSTLYNSVSESEILNATLTFPIIYDNLRAE--VFNYRFPFKGSL

HP FFL-LGEECAQKIRALVDHHDADAEVKEKVVIIIPKI

KI FYLCTTSGVCVKIKIRALANHHHDLTVKVKIKILVKNKF

20 Furthermore, the search of the Genbank using the base  
sequences of the present cDNA has revealed the registration  
of sequences that shared a homology of 90% or more (for  
example, accession No. N92228) in ESTs, but, since they are  
partial sequences, it can not be judged whether or not any  
of these sequences codes for the same protein as the protein  
of the present invention.

25 <HP10540> (SEQ ID Nos. 38, 48, and 58)  
Determination of the whole base sequence of the cDNA  
insert of clone HP10540 obtained from cDNA library of human  
osteosarcoma cell line Saos-2 revealed the structure

consisting of a 47-bp 5'-untranslated region, a 297-bp ORF, and a 245-bp 3'-untranslated region. The ORF codes for a protein consisting of 98 amino acid residues and there existed two putative transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CEF49C12.12 (GenBank Accession No. Z68227). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CEF49C12.12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.1% in the entire region.

Table 11

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25	HP M-ASLLCCGPKLAACGIVLSANGVIMLIMLGIFPNVHSAVLIEDVPFTEKDFENGQNIY
	*        ***   *   *   *   *   *   *   *   *   *   *   *
	CE MGKICPLMGPKMSAFCMVMSVWGVI FLG LLGVFFYIQAVTLFPDLHF-EGHGKVPSSVID
	HP NLYEQVSYNCFIAAGLYLLGGFSFCQVRLNKRKEYMVR
	*        *        *        *        *        *
30	CE AKYNEKATQCWIAAGLYAVTTLIAVFWQ---NKYNTAQIF

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. AA420715) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

10 <HP10557> (SEQ ID Nos. 39, 49, and 59)  
 Determination of the whole base sequence of the cDNA insert of clone HP10557 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 24-bp 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-untranslated region. The ORF codes for a protein consisting of 172 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was larger than the molecular weight of 18,844 predicted from the ORF. In this case, the addition of a microsomal fraction led to the formation of a product of 39 kDa which is considered to have been subjected to some modification after secretion. In addition, there exist in the amino acid sequence of this protein no site at which N-glycosylation may occur. Application of the (-3',-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 32. When expressed in COS7 cells, an expression product of about 20 kDa was observed in the supernatant fraction and the membrane fraction.



15

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HP                                                                    MVGPAP

PG MAAGDGDVKLGTLSGSGESSNDGGSESPGDAGAAAEGGGWAAAAALALLTGGGEMLLNVAL
HP RRRRLRPLAALALVALALAPGLTARAGQTPRAERGPV--RLFTEEELARYGEEEDQPI
20      * * * * *
PG VALVLLGAYRLWVRWRRGLGAGAGAGEESPATSLPRMKKRDFSLEQLRQYDG-SRNRP
HP YLAVKGVVFDVTSGKEFYGRGAPYNALTGKDSTRGVAKMSLDPADLTHDTTGLTAKELEA
      * * * * *
PG LLAVNGKVFDVTGSGKFYGPAGPYGIFAGRDASRLATFCLDKDALRDEYDLSDLNAVQ
25 HP LDEV--FTKVYKAKYIVGYTARRILNEDGSPNLDFKPEDQPHFDIKDEF
      * * * * *
PG MESVREWEMQFKEKY---DYVG-RLLKPGEEPS-EYTDEEDTDHKNQD

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30 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AAI01709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10563> (SEQ ID Nos. 40, 50, and 60)  
 Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (Genbank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A. thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.5% in the entire region.

Table 13

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HP MMPSRTNLATGIPSSKVKYSRLSSTDGVIDLQFKKTPPKIPYKAIALATVLFILGAFLI
      *..* *. . . . * *.**..* ..... *
5  AT      MAYVDHAFSISDEDLMIGTSY-TVSNRPPVKEISLAVGLLVFGTLGI
HP IIGSLLLSGYISKGGADRAVPVLIIGILVFLPGFYHLRIAYYASKGYRGYSYDDIPDFDD
      ..* .. . . . *. .... ..* *.**..* .....* *.**..* .....*
AT VLGFFMAYNRVG-GDRGHGIFIVLGCLLFIPGFYTRIAYYATKGYKGFSFSNIPSV

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10

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA083574) in ESTs, but, since they

15 are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01467> (SEQ ID Nos. 61, 71, and 81)

20

Determination of the whole base sequence of the cDNA insert of clone HP01467 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 65-bp 5'-untranslated region, a 924-bp ORF, and a 447-bp 3'-untranslated region. The ORF codes for a

25 protein consisting of 307 amino acid residues and there existed three putative transmembrane domains. Figure 21 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation

30 product of high molecular weight.

The search of the protein data base using the amino

acid sequence of the present protein revealed that the protein was similar to the rat Sec22 homologue (Genbank Accession No. U42209). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat Sec22 homologue (RM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 94.6% in the N-terminal region of 241 amino acid residues. The protein of the present invention was longer by 53 amino acids at the C-terminus than the rat Sec22 homologue.

Table 14

15	
20	HP MSMTLSASVAVVRDGLPLSASDTRDQSGTGMDGECRKYFKKLSRKKLALQDPRCTLTGTHYNI *****. HP NFISSLSGVSNMGLCTENYPNVLAASFSLDELQKEEFTTYNMKMTNVAVRPCFIEPDNFIO ***** HP NFISSLSGVSNMGLCTENYPNVLAASFSLDELQKEEFTTYNMKMTNVAVRPCFIEPDNFIO ***** HP RTQRNNYNNRSLSTTKINLSDMQTEIKLRPPYQISMCETLGSANGVTSAFSDCKGAGAKISS ***** HP RTQRNNYNNRSLSTTKINLSDMQTEIKLRPPYQISMCETLGSANGVTSAFSDCKGAGAKISS ***** HP AHQRTLPATLSGIVGFIILSLTSGALNLIHGFHAIESILSDGDDPNYIIAFLTGLTAACLY ***** HP AHQRTLPATLSGIVAFIILSLTSGALNLIHGFHAIESILSDGDDPNYIIAFLTGLTAACLY ***** HP AHQRTLPATLSGIVAFIILSLTSGALNLIHGFHAIESILSDGDDPNYIIAFLTGLTAACLY ***** HP QCYTLVYVYTTGWRNWKSFLLTFGLICLCNMWLYTELNLWGLFPHVTVGAFVTLQIWLIRQAQG ***** RM QMTCICLQGRKERT

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA421925) in ESTs, but, since they  
5 are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01956> (SEQ ID Nos. 62, 72, and 82)

10 Determination of the whole base sequence of the cDNA insert of clone HP01956 obtained from cDNA library of human liver revealed the structure consisting of a 86-bp 5'-untranslated region, a 552-bp ORF, and a 359-bp 3'-untranslated region. The ORF codes for a protein consisting  
15 of 183 amino acid residues and there existed one putative transmembrane domain. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product  
20 of 20.5 kDa that was almost identical with the molecular weight of 20,073 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the yeast hypothetical protein 21.5  
25 kDa (SWISS-PROT Accession No. P53073). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the yeast hypothetical protein 21.5 kDa (SC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that  
30 of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

of 34.3% in the C-terminal region of 108 amino acid residues.

Table 15

5	HP	MTAAGGLVANNRGRFRKFWAIELSGPGGSGRGRSDRSGSGGDSLVPGVYLDKQVPTDS
10	SC	MSRGEPFEWAKKHLLDPTKYIEKKNINQNSNTLPSPGFEGRSSSKGNVTRKQDPAATSGTSLA HP VQETDRILVEKRCWDIALGELTKQIIPNNLPIIMYMAGNTISIFPTMVCMMARPIQALMAI SC QKNQITVLQVQAKAMQIALGPAKSIPIPNIMFMSYMSGTSLQIIPIMTALMLSGPIKAIATST HP SATPK--MLTESSSQKFIQGLGLVLYLIGNLIMGIALAV-Y-KQSGMGLLPHTHAPDIAFIEPPE .....* * * * * SC RSAPKPIVLGNKKAATQSQVQVQTAEMEWYIVFQGVLMYIGYRKLTNSMGLIPINAKGDWLPWERIAH HP RMERSGGGLTL
15	SC	YNNGLQWFSD

20 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAL59753) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

25 protein of the present invention.

<HP02545> (SEQ ID Nos. 63, 73, and 83)  
determination of the whole base sequence of the cDNA insert of clone HP02545 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 133-bp 5'-untranslated region, a 984-bp ORF, and a 636-bp 3'-untranslated region. The ORF codes for a

30

protein consisting of 327 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat embigin (EMBL Accession No. AJ009698). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat embigin (RN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 65.4% in the entire region.

Table 16

5	HP MRALPGLEARARTRPRLTLQCLLAARPSADGAPDPSPTSPPLREIMAN--NFSLE RN MSHGTGLRALVAPGCSITLT--YLAATRPDAVADPADSAFTSLPVEREMMKYANISLE HP SHNISLTSHSSMPVERKNITLERPSNVNLTQQTTSGLDNAVNVTWKKDGEOLE--NNYLV ..... RN TYNISLTBOQTVAS--RQNTITLERPSHLEECFTFATLEDVMSNMVNTWKKDALTLETTDGFT HP SATGSLTYLTQYRFRFTIINSKKQMSYSCFFREKEKEQRRGTNFNKVPELHGKMKPLISYVGDST RN LKMGDTLYSQRFRFTVFNSSKQMSYSCFLGEE--LRGTNINIRKVPKRVHKGKMKPLITYVGDST HP VLTCKQCQNCPEPLNMWTWYSSNGSVKVPVGVOH--NKYVINGTYANETKTKITQTLLEDGESY ***** RN VLKCEQCQNCPLNMWTWYSSNGTAQVPIDVHVNKDFDINGSYANETKTKKAKHLLLEDGESY HP WCRATFQTLGSESEHIEIETVLSYLVAPLKPFLLVIAVAEVLILVAITLTCCKKQKKHSDG ***** RN WCRAPPLIGSESEHIEIKIKLVLSFMVAPLKPFLLVIAEVLILVAITLTCCEVYTQKKKNPDDE HP KEFQIETQTLKSDSDSNGIENNVPFRHKKNEISLQ ***** RN KEFQIETQTLKSDSDSNGIENNVPFRYKRTDSDGQ
10	
15	
20	

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA312629) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02551> (SEQ ID Nos. 64, 74, and 84)  
Determination of the whole base sequence of the cDNA insert of clone HP02551 obtained from cDNA library of human



osteosarcoma cell line Saos-2 revealed the structure consisting of a 61-bp 5'-untranslated region, a 672-bp ORF, and a 384-bp 3'-untranslated region. The ORF codes for a protein consisting of 223 amino acid residues and there  
5 existed a putative secretory signal at the N-terminus. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was somewhat larger than  
10 the molecular weight of 24,555 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 26 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the  
15 secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 20.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse FGF binding protein  
20 (GenBank Accession No. U49641). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse FGF binding protein (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the  
25 protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 21.2% in the entire region other than the N-terminal region. In particular, all the eight cysteine residues contained in the  
30 both proteins were conserved.

30 Determination of the whole base sequence of the cDNA  
 insert of clone HP02631 obtained from cDNA library of human  
 osteosarcoma cell line Saos-2 revealed the structure  
 consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,  
 <HP02631> (SEQ ID Nos. 65, 75, and 85)

25 protein of the present invention.  
 any of these sequences codes for the same protein as the  
 are partial sequences, it can not be judged whether or not  
 example, Accession No. A317400) in ESTs, but, since they  
 of sequences that shared a homology of 90% or more (for  
 sequences of the present cDNA has revealed the registration  
 Furthermore, the search of the Genbank using the base

15 MM SWSISCTTFPLNMLQATSC  
 HP PQAALCAFLISFFNG  
 MM RHNKNVQAVSTSPNRKIKEDI-TLNPAATQTM-TIRDPCECLDPPDLNQ-RKTALFECEG  
 HP SLRPKATVKLTLEATQTLGKDSMEELGKAKKPTTRPTAKPTQPGPRPGGNEAKKKAKWHEHCWK  
 MM IYKQVARTLRKQKNICRDAAKSVLTKTRVCCKRFPESNLKTLVNPNAARGNTKPRKAEKAVSA  
 10 HP SYWNAQLEIRNLHNAAGQA-PVLRPSVCSREAGPQAHMQGVTSLSLKSGSPNQPEAGTP  
 MM LTHGKFTVKDQATC---RMAVTEEEGGISLSIKVQCTQADQEFSCVFAADPTDCLKKHDKD-Q  
 HP GEEHFHFGGRDSCTMRRPSSLGQAGAEVWLRVDCCRNITDQTYWCERYRQPSMCQAFAADPK  
 5 MM MLTHSLIILLTSLTLLATQAFSEKVRKRRKAKNAPHSIAEKGVEGASAPSLGKAQNKQKRSRSTKS  
 HP MKFVPCLLTLVTLSCLSTLGAAPRQKQGST

Table 17

and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAL56969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

elephantine hypophyseal protein CR2212 (CB). Therefore, the two human proteins of the present invention (H1 and H2) shared a homology of 51.4% in the entire region.

Table 18

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CE NITLPIINTSIHANACRMWCLICCGEDSELIRYEDGDEHTHMA
30
HP LSHGRPLAESESEÖERTLTGTRTIPINDAS
CE TKELSAITRMVLDISVRLTIVWVSLPILRHEKFAITAIÖLÖSGFAMLITGLIYINDILIGPWR
*****
HP TKELSAITRMVLDISLRTVIVWVSLTALGWFBAFHALÖILGFLITLITGATLYNGTHRPLGR
CE IIMIPFYIIVHPPESTNPEBERLEDVFAKMEKTEEPITATLSGVTSIAFNFAGVSA
*****
HP IITVPMYIIPAG-SFSGNPRGTLTEDADPAFCÖGÖÖPLIIVALTGNISIAFNFAGVSI
CE YDDPDLÖKNAITIGLIT.IIWAÖIIVAIÖMWYÖKILTKIKDVSALPAVAGTEGTLGAVMLT
*****
HP SKHDÖHÖKLTSEVITGDLITIMAOIIVAIÖMWLEKFKFYKXNHVHPLRAVÖTEGTLGAVMLT
CE MYIGLITLITPSSÖMTBAAVITFITGTLVGNIMAOIKPKFFKFMFLFVMLGAVITGAVDLY
*****
HP MYVALNMTSASÖPÖMTBKGAVITFIFGÖLFSVAFILGRBLVLSÖMLGILITITAGVVLVGLADLT
CE CTAVFELIFGFKRYVMNBAVNOGESATBELITEKKEPFLIPBNPPLFPPALCÖIIGTSI
*****
16
HP CIIAPYLT-----LTCBAQÖSS-----SVDPÖGFNPLFLPPLCÖMTGTSI
CE NVAPAYIISVMVTVTSITLITICAMADS IKAD-----GVFNNHPLPÖATCMFPGEFL
*****
HP MAMTYÖLÖFLAGLITLVTGTSINTLSAKWADNFMKRGCGGSKESHFÖHPÖLÖAVGMGFLGFS

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N50907) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10488> (SEQ ID Nos. 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10488 obtained from cDNA library of human liver revealed the structure consisting of a 39-bp 5'-untranslated region, a 273-bp ORF, and a 421-bp 3'-untranslated region. The ORF codes for a protein consisting of 90 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,151 predicted from the ORF. When expressed in COS7 cells, an expression product of about 6 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H73534) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10538> (SEQ ID Nos. 68, 78, and 88)

determination of the whole base sequence of the cDNA insert of clone HP10538 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 357-bp 5'-untranslated region, a 1500-bp ORF, and a 1911-bp 3'-untranslated region. The ORF codes for a protein consisting of 499 amino acid residues and there existed at least four putative transmembrane domains. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse pore-forming K<sup>+</sup> channel subunit (Genbank Accession No. AF056492). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse pore-forming K<sup>+</sup> channel subunit (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 32.4% in the N-terminal region of 241 amino acid residues.

Table 19

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HP  MVDRGPLLTSAIIFYLAIGA AIFEVLEEPHWKEAKKNYYTQXHLHLEKFPCLGQEGLDK
      * . . . . . ** . . . . . * . . . . . . . . . . * . . . . .
5  MM MRSTLLALLALVLLYLVS GALVFQALEQPHEQQAQKMDHGRDQFLRDHPCVSQKSLED
HP  ILEVVS DAAGQG-----VAITGNQTFNNWNWPNAMIFAATVITITIGYGNVAPKTPAGRLF
      . . . . . * * * . . . . . ** . . . . . * . . . . . * . . . . .
MM  FIKLLVEALGGGANPETS WTNSSNHS SAWNLGSAFFFSGTIITITIGYGNIVLETDAGRLF
HP  CVFYGLFGVPLCLTWISALGKFFGGRAKR----LGQFLTRKGVSLRKAQITCTVIFIVWG
10  * . . . . * . . . . . . . . . . * . . . . . * . . . . . * . . . . .
MM  CIFYALVGIPLEFGMLLAGVGDRLGSSLRRGIGHIEAIFLKWVPPGLVRSLSAVLFLLLIG
HP  VLVHLVIPPFVFMVTEGWNYIEGLYYSFITISTIGFGDFVAGVNPSPANYHALYRYFVELW
      * . . . . * . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
MM  CLLFVLTPTFVFSYMESWSKLEAIYFVIVTLTIVGFGDYVPG-DGTGQNSPAYQLVWFW
15  HP  IYLGAWLSLFWNVKVS MFVEVHKAIKRRRRRKESFESSPHSRKALQVRGSTASKDVNI
      * . . . . .
MM  ILFGLAYFASVLTITIGNWLRVSRRTAEMGGLTAQAASWTGTVTARVTRTQGPSAPPE

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20 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R25184) in ESTs, but, since they are partial sequences, it can not be judged whether or not any

25 of these sequences codes for the same protein as the protein of the present invention.

<HP10542> (SEQ ID Nos. 69, 79, and 89)

Determination of the whole base sequence of the cDNA

30 insert of clone HP10542 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 23-bp 5'-untranslated region, a 321-bp ORF, and a 426-bp 3'-

untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,724 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA029683) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10571> (SEQ ID Nos. 70, 80, and 90) determination of the whole base sequence of the cDNA insert of clone HP10571 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 95-bp 5'-untranslated region, a 459-bp ORF, and a 675-bp 3'-untranslated region. The ORF codes for a protein consisting of 152 amino acid residues and there existed one putative transmembrane domain. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20 kDa that was larger than the molecular weight of 17,062 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 23 kDa



which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ile-Thr at position 10).

- 5        Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAL05822) in ESTs, but, since they are partial sequences, it can not be judged whether or not  
10 any of these sequences codes for the same protein as the protein of the present invention.

<HP01470> (SEQ ID Nos. 91, 101, and 111)

- 15        Determination of the whole base sequence of the cDNA insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative  
20 transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight  
25 of 40,489 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to have been subjected to some modification. Application of the  
30 (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 23. When

expressed in COS7 cells, an expression product of about 44

kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the

protein was similar to the Caenorhabditis elegans hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP)

and the C. elegans hypothetical protein 39.9 kDa (CE).  
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Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The  
15  
both proteins shared a homology of 58.9% in the entire region.



5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-untranslated region. The ORF codes for a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0108 (SWISS-PROT accession No. Q15012). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0108 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.9% in the entire region.

Table 21

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	HP	MKMVAPWTRFYSNSCCLCCHVRTGTILLGVWYLIINAVVLLILLSALADPD---QY
		*****
5	KI	MVMSFMRNRSDRFYSTRCCGCHVRTGTIILGTWYMVVLLMAILLTVEVTHPNSMPAV
	HP	NFSSSELGGDFEF-MDDANMCIAIAISLLMILICAMATYGAYKQRAAWIIPFFCYQIFDF
		*. . . *
	KI	NIQYEVIGNYSSERMADNACVLFAVSVLMFIISMLVYGAIISYQVGNLIPFFCYRLPFD
	HP	ALNMLVAITVLIYPNSIQEYIRQLPPNFPYRDDVMSVNPCTCLVLIILLFISIIITFKGYL
10		*. ****. * * . * . * . * . * . * . * . * . * . * . * . * . * . * . *
	KI	VLSCLVAISSLTYPRIKEYLDQL-PDFPYKDDLALDSSCLLFIVLVFFALFIIFKAYL
	HP	ISCVWNCYRYINGRNSSDVLVYVT-SNDTTVLLPPYDDATVNGAAKEPPPPYVSA
		*.*****.***. . . * . . . * . * . * . * . * . * . * . *
	KI	INCWVNCYRYINNRNVPEIAVYPAFEAPPQYVLPTY-EMAVKMPKEPPPPYVLP

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA173214) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP02631> (SEQ ID Nos. 93, 103, and 113)

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 588-bp ORF, and a 750-bp 3'-untranslated region. Although the 49th amino acid residue is encoded by a stop codon, it is likely that this codon encodes selenocysteine from the molecular weight

of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translocation product of 58 kDa. In this case, the addition of a microsomal fraction to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the C-terminal region. Cysteine was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

Table 22

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	HP	MRLLLL
5	CE MRIHDELQKQDMSRFGVFIIGVLFFMSVCDVLRTEESHSDENHVHEKDDFEAEFGDETD	
	HP LLVAASAMVRSEASANLGGVPSKRLKMQYATGPLLKEQICVSUGYRRVFEEYMRVISQRY	
		* * * * *
	CE QSFSQGTEDHIEVREQSSFVKPTAVHHAKDLPTLRIFYCVSCGYKQAFDQFTTFAKEKY	
	HP PDIRIEGENYLPQPIYRHIAFSLVFKLVLIIGLVGKDPFAFFGMQAPSIWQWQENKV	
10	* * * * *	
	CE PNMPIEGANFAPVLWKAYVAQALSFVRMAVLVLVGGINPFRFGLGYPQILQHAHGKMK	
	HP YACMMVFFLSNMIEQCMTGAFETLNDVPVWSKLESCHLPSMQQLVQILDNEMKLNHV	
		* * * * *
	CE SSCMLVFMLGNLVEQSLISTGAFEVYLGNEQIWSKIESGRVPSQEFMQLIDAQLAVLGK	
15	HP MDSIPPHRS	
	CE APVNTESFGEFQQT	

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20 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not

25 any of these sequences codes for the same protein as the protein of the present invention.

<HP02695> (SEQ ID Nos. 94, 104, and 114)

Determination of the whole base sequence of the cDNA insert of clone HP02695 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 112-bp 5'-untranslated region, a 1020-bp ORF, and a 160-bp 3'-

30

untranslated region. The ORF codes for a protein consisting of 339 amino acid residues and there existed three putative transmembrane domains. Figure 34 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 38 kDa that was almost identical with the molecular weight of 38,274 kDa predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat hypertension-induced protein S-2 fragment (PIR Accession No. 539959). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat hypertension-induced protein S-2 fragment (RN). Therein, the marks of \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.3% in the entire region.



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by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Caenorhabditis elegans hypothetical protein CELK07H8 (Genbank Accession No. AF047659). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C. elegans hypothetical protein CELK07H8 (CE). Therein, the marks of '-', '\*' and '.' represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.2% in the entire region.



example, Accession No. A4334000) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10530> (SEQ ID Nos. 96, 106, and 116)

determination of the whole base sequence of the cDNA insert of clone HP10530 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 80-bp 5'-untranslated region, a 1182-bp ORF, and a 95-bp 3'-untranslated region. The ORF codes for a protein consisting of 393 amino acid residues and there existed a putative secretory signal at the N-terminus.

Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 46 kDa that was somewhat larger than the molecular weight of 44,912 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 45.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1)-rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 23. When expressed in COS7 cells, an expression product of about 43 kDa was observed in the supernatant fraction and the membrane

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein IG02N01 (Genbank Accession No. AF007269). Table 25 shows the comparison between amino acid sequences of the

human protein of the present invention (HP) and the A.  
thaliana hypothetical protein IG002N01 (AT). Therein, the  
marks of -, \*, and . represent a gap, an amino acid residue  
identical with that of the protein of the present invention,  
5 and an amino acid residue similar to that of the protein of  
the present invention, respectively. The both proteins  
shared a homology of 27.0% in the N-terminal region of 355  
amino acid residues.

30 Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. A302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

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 20  
 15  
 10  
 5  
 HP  
 NRTLENTLMT

AT MELTSPKSPSSNDVVSFSLVHNSMARRRRSSAAESLKKRRNDGESLCCQVVGQDSRR  
 HP ALACSPVHTTLLSKSDAKKAKSKTLLKESQFSDEKPVQDRGLVTDTLKAESVVLGRYCSA  
 AT LTITFVFIPIPAVSIAVYKAKFADRNVIQTESSIHQKGIKVTIDINFGIILTEHSK--AS  
 HP KARDHAFAGDVLGIVTPMNSHGVDVTKVFGSKFTQISPVWLQ-LKRRGRNREVEVGLGADV  
 .....  
 AT ENSTRHNDYPVALAITYP--CQSGT--VLEGR-HNADKGMVQIEILSRGNALSASKGLPKL  
 HP DQGMRAVAVKHKAKGHLHIVPRLLFEEDWTYDDPRNVLDSEDEIEELSKTVVQVAKNQHGDFG  
 .....  
 AT ---INSCIFHALKRMNFEFTLETNVNNTYTLVIMFALNS-REMEYNGIIVLESWRMAAYGLV  
 HP VEVWNQTLTQKRVGLIHMLTLHAEALHQARLTALLVIPPAITPQDGLQMEFTHKEEJOL  
 .....  
 AT HDPIKMAKATKFKVQKQGLDGLAHSTSSPRNNQGMFMVAVVGPFRSEKTLQMYDQFEDJOL  
 HP AVPLDGFSLMTYDYSIAHQGPBNAPLSWVRACVQ-VLDPKSK-----WRSKILLGLGNFYGM  
 .....  
 AT KQVDGESLMTYDESINPQNPAPVKNWIDLTLTKLLTSSNNINDSNIARKKVLLGINFYGN  
 HP DYATSKDAREPVGARXYIQTLDKDRPRMVMWDSQASHEFFEEKKRSGRHVFPYFLKSLQ  
 .....  
 AT DVISGGGCAITGRDYLTALTQKHKPTFPWDXKESGEHLFMYRDPDKNIKIKHNAVFPYFLMSLI  
 HP VRTIARELGAVGVSIWELTGGGLDYFDLL  
 .....  
 AT LLENARLTWIGIISWELGQDKGHEGKYAEASLEASSISFGHTFDMQFRNTPRQLSRNGS

Table 25

protein of the present invention.

<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA  
5 insert of clone HP10541 obtained from cDNA library of human  
stomach cancer revealed the structure consisting of a 7-bp  
5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-  
untranslated region. The ORF codes for a protein consisting  
of 196 amino acid residues and there existed a putative  
10 secretory signal at the N-terminus. Figure 37 depicts the  
hydrophobicity/hydrophilicity profile, obtained by the Kyte-  
Doolittle method, of the present protein. In vitro  
translation resulted in formation of a translation product  
of 23 kDa that was somewhat larger than the molecular weight  
15 of 21,553 predicted from the ORF. In this case, the addition  
of a microsome led to the formation of a product of 20 kDa  
from which the secretory signal is considered to have been  
cleaved and a product of 23 kDa which is considered to have  
a sugar chain being attached. Application of the (-3,-1)  
20 rule, a method for predicting the cleavage site of the  
secretory signal sequence, allows to expect that the mature  
protein starts from glycine at position 41. In addition,  
there exists in the amino acid sequence of this protein one  
site at which N-glycosylation may occur (Asn-Leu-Thr at  
25 position 185).

The search of the protein data base using the amino  
acid sequence of the present protein revealed that the  
protein was similar to the human zymogen membrane protein  
(GenBank Accession No. AF056492). Table 26 shows the  
30 comparison between amino acid sequences of the human protein  
of the present invention (HP) and the human zymogen membrane  
protein (ZM). Therein, the marks of -, \*, and . represent a

gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.6% in the C-terminal region of 133 amino acid residues.

Table 26

10	HP MWRVPGTTRRPVVTGTSPPGMHRPPEAMLLTLTLALLGPPFWAGKMYGPGGGKYYTS-TTEDYD ZM ***** ZM LTLVATLALTLCAASAGNATIQARSSSSYSYSGEYSGGGGKRFTSHSNGQLD HP HEITGLRNVASVGLLVKSVQVKLGDSWDVKLGALGNTQEVTLPGEGEYITKVFVAFQAFLR ZM ***** ZM GPITATLRVNTYYIVGLQVRXYGKWSMDYGVGNMGDLREIIFLHPGESVIVQSGKYKWTLK HP GMYWYTSKXDYYEYFGKLDGQISSAYPSQEGQVLVGLVGIYQQLLGKIKSIGFEWN-YPLERP ZM KLVETVTDKRGKRYLRFKSDSGTSFNNAVPLHPNVTWIFRISGRSGSL-IDALIGLHWDDVYPTSCS HP TTEPPVNLITYSANSPPVGR
20	ZM RC

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10550> (SEQ ID Nos. 98, 108, and 118)  
determination of the whole base sequence of the cDNA



insert of clone HP10550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 241-bp 5'-untranslated region, a 324-bp ORF, and a 86-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA348310) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10590> (SEQ ID Nos. 99, 109, and 119)

Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

Determination of the whole base sequence of the cDNA  
5 insert of clone HP01462 obtained from cDNA library of human  
fibrosarcoma cell line HT-1080 revealed the structure  
consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF,  
and a 477-bp 3'-untranslated region. The ORF codes for a  
protein consisting of 483 amino acid residues and there  
10 existed a putative secretory signal at the N-terminus.  
Figure 41 depicts the hydrophobicity/hydrophilicity profile,  
obtained by the Kyte-Doolittle method, of the present  
protein. In vitro translation resulted in formation of a  
translation product of 72 kDa that was larger than the  
15 molecular weight of 55,838 predicted from the ORF.  
Application of the (-3,-1) rule, a method for predicting the  
cleavage site of the secretory signal sequence, allows to  
expect that the mature protein starts from lysine at  
position 21.

20 The search of the protein data base using the amino  
acid sequence of the present protein revealed that the  
protein was similar to the *Caenorhabditis elegans*  
hypothetical protein ZK1058.4 (EMBL Accession No. Z35604).  
Table 27 shows the comparison between amino acid sequences  
25 of the human protein of the present invention (HP) and the *C.*  
*elegans* hypothetical protein ZK1058.4 (CE). Therein, the  
marks of -, \*, and . represent a gap, an amino acid residue  
identical with that of the protein of the present invention,  
and an amino acid residue similar to that of the protein of  
30 the present invention, respectively. The both proteins  
shared a homology of 35.6% in the entire region.

30	CE	-KSPKQK0LTKVK
		*****
	HP	KKKKKKQIKVKKM
	CE	KKEFEADQK0TQ0FQ0RA0V0ARREBEKTRERKKQK0LMDSESDPER0KRLTBAKELKREAKA--
25	HP	RAVAVENETLKI.TLV0Q0R0A0SRRERKKRAKKEIRINNEDEPEK0RRLTEAATRRER0KRLTE
	CE	-RLP0A0R0MYEVSINL0YLQ---Q0EVSMEIILNVLVLYLIDKARMKLSDKAVKAKRER
		*****
	HP	LKLPDQKRLTLPTNPPGSGGLTPPKMRETLPTLNMVAVISIDAKKFFILNBRG0KQ0AKKN
20	CE	A0Q0FLNPAWQVAD0NEVVEISILDPGVASLTLKKEHDAIEIFIHISIDQTLGP0KABEGEYLT
		*****
	HP	GAKYGLPDSLALISENGEVEUTKMMVHFLTHYADKIESVHFS0QSGKIN0EG0P
	CE	VSRIEMETPESGDKMILIKASLLETNTDPLIFAVGEKKIASKFKEMDLNDSAPSERQ0A
		*****
15	HP	INVLARMARPAVS0VQIKVTNM--DEMDYLVFVAGTRKALVRL0KEMQDLSF0CS0DKPKS
	CE	CRPLTE0R0AVAV0DEQTL0KIPISLTKHNDPLDS0AMCTGRVNVNSLFL0KMKV0K0DV
		*****
	HP	HR0ELTESNLTLV0BDG0TKNKEATST0GKTLN0GENEHI1NYLM0SGR0V0CCE0MIL0TLRFLK0DL
	CE	S0DA0A0Q0LTKFAD0V0A0HFR0ANNS0AS0Y0L0IILMTNLTIL0GKTLTNSI0AQ0ITPDM
10		*****
	HP	TSSSKNK0PDI0VD0PAH0L0NSWESY0L0IILMT0GLT0LAINVYI0GKNKNSR0L0AQ0M0NT
	CE	D0NEF0E0F0E0F0E0SS0AT0A0E0I0Q0R0E0P0V0IK0K0D0F0E0R0E0D0F0V0E0E0R0E0K0V0R0E0AD
		*****
	HP	ED0E--DETTLVRL0E0Q0DEN0GE0DE0AD0T0E0G0E0T0E0P0E0Y0E0DE0F0E0G0ED0P
	CE	KMIWIMILIFIFIG0AIST
		*****
	HP	MKAFH0TLFCV0LTLF0GSVSEAKF0DF0E0DE0D0I0VE0VDND0P0AF0E0D0M0E0D0VS0E0SP0R0V0IIT

example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5

<HP02485> (SEQ ID Nos. 122, 132, and 142)

Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein W01A11.2 (GenBank Accession No. U64852). Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein W01A11.2 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

Table 28

HP MVEFAPLPMWERRRLQTLAVLQVFFSFLALAEICQ-A

CE MRLTSLTSSISGAKALPDKELCSSVSRIILAPLTVPWKRLRLTTLAVMGFIWMVLTINDLV

HP GFIALTLFTREFWLLTVLYAAMWYLLDRLDKPRQGGRRHIQAIRCWITWIKMYKMDYVPSISLVKTAKE

CE PFHLVFNTRMWFLVPLVLYAWFYDYDPTPKKASRRNMWARRHVAWKYFASVFPPLIKIKITAD

HP LDPSRNYIAGHPHGHGVLAVGAVANLCTESLTSGLSSIPPGIRPHLMMLTLWFRAPAPPRDYIM

CE IPADRNRYIIGSHPHGMFSVGGFTAMSTNATGFEEDKFPFGIKSHIMTINLNGGYTFPPRRERGI

HP SAGLVTSERESASAHILNRKKGGNLGLIVGAGQALDARPGSPFTLLLRNRKGFVRALALTH

CE MLGIEIVSKESLEYLLTTCGKGRACALIVIGASALAEALHAPNKNNTLTLLINRRHGFCKYATKAF

HP GAVLPVIFSFGRNDLTFDQIPNNSGGSWLRKYIQNRLQKIMGISLPLFHGRGVF-QYSGELIP

CE GADLVPMVNFGENDLTRYQENPKGSRIRREVQEKIKDMFGLCPPLLRGRSLFNQYVLTIGLTP

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

CE FRKPVTWNGRPRIKVTQTDPEPTEVEQIDELHAKYKCDALYTNLFEELYKHHLHSIPPDTHLIFQ

HP YRRPILTIVVGKPIEVQKTLHPSEEEVNOHLHQRYIKIKELCNLTFEAKHKLKFKNIPADQHLERC

insert of clone HP02798 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 31-bp 5'-untranslated region, a 804-bp ORF, and a 301-bp 3'-untranslated region. The ORF codes for a protein consisting of 267 amino acid residues and there existed four putative transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 30,778 predicted from the ORF. When expressed in COS7 cells, an expression product of about 26 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human DHHC-containing cysteine-rich protein (GenBank Accession No. U90653). Table 29 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human DHHC-containing cysteine-rich protein (DH). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.0% in the intermediate region of 100 amino acid residues. The positions of seven cysteines were conserved between the two proteins. The protein of the present invention also had the DHHC (Asp-His-His-Cys) sequence.

Table 29

HP	MAPWALTSPGVLTVRTIGHTVLTWGI
5	DH MYKMNICNKPSKNTAPAEKSVWTAAPAQSGSPFELQGGQRSRNCGMSWPPHPIQIWAAILYL HP TLVILFLHIDTELKQWERQGGELTLPTLTLVTLVLSLMDPQYVNVGPQ-QEELK * * * * * DH PPAVIGFGLVPLTPHHHWPVAGYACMGAIFFAGHLLVTHLTAVSISDPAADNVRDKSVYAGLPL HP EQGTAVPPAPPLRRCGRYCLVLQPLRKARHCRCRCRCVRKYDHNHCPRWENCVCGRNHPFLV * * * * * DH IFNRSGHMAHVIEDLHCNLDVDSABSKHCSACNKCKVCQGFDDHNCWKMLNNCQGVGRNRYPL HP VYIALQVLVLIMWGLYIAWSGRLRFQFWGLMWLRSSGILFATPFLTLISLFSVLASLTLVSHLY * * * * *
10	DH HSASALTCVLTLLVIGGHICLRGVLCPHSAHQPTL
15	

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. D79050) in ESTs, but, since they are of these sequences codes for the same protein as the protein of the present invention.

<HP10041> (SEQ ID Nos. 124, 134, and 144)  
determination of the whole base sequence of the cDNA insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts



the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

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	HP	MSTNNMSDPRPRPNKVLRYKP---PPSECNPALDDPTPDYMNLLGMIFSMCGLMLKLKWA
		.....*..... .. .. ** *.***.....*
25	CE	MQQNGDPRRTNRIVRYPKPLDSTANQQQAISEDPLPEYMNVLGMIFSMCGLMIRKMKWCS
	HP	WVAVYCSFISFANSRSSEDTKQMMSSFMLSISAVVMSYLQNPQPMTPPW
		*.*. ** *****.*.*.*.....*
	CE	WLALVCSCISFANTRTSDDAKQIVSSFMLSVSAVVMSYLQNPSPPIIPVWVTLQTS

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30

Furthermore, the search of the GenBank using the base

5 sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10246> (SEQ ID Nos. 125, 135, and 145)

10 Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translaton product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

25 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (Genbank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

5

Table 31

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HP MTLFHFNGCFALAYFPYFITYKCSGLSEYNFWKCVQAGVTYLFVQLCKMLFLATFFPTW
*****
TM MTLFHFNGCFALAYFPYFITYKCTDLSEYNFWKCVQAGVTYLFVQLCKMLFLATFFPTW
10 HP EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
*****
TM EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
HP VGARGIEFDWKYIQMSIDSNISLVHYIVASAQVNMITRYDLYHTFRPAVLLMLFLSVYKA
*****
15 TM VGARGIEFDWKYIQMSIDSNISLGPYIVASAQVNMITRYDLYHTFRPAVLLMLFLRVYKA
HP FVMETFVHLCSLGSAALLARAVVTGLLALSTLALYVAVVNVHS
*****
TM FVMETFVHLCSLGSAVLMAGVVVKGLLVIRNLAMYVAVVNVHS

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20

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25

<HP10392> (SEQ ID Nos. 126, 136, and 146)

30

Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

consisting of a 24-bp 5'-untranslated region, a 77-bp ORF, and a 76-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

<HP10489> (SEQ ID Nos. 127, 137, and 147)  
 Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10519> (SEQ ID Nos. 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

30 depicts the hydrophobicity/hydrophilicity profile, obtained transmembrane domain in the intermediate region. Figure 50 secretory signal at the N-terminus and one putative of 428 amino acid residues and there existed a putative untranslated region. The ORF codes for a protein consisting 5'-untranslated region, a 1287-bp ORF, and a 1276-bp 3'-stomach cancer revealed the structure consisting of a 210-bp insert of clone HP10574 obtained from cDNA library of human 25 Determination of the whole base sequence of the cDNA <HP10574> (SEQ ID Nos. 130, 140, and 150)

of the present invention.

20 of these sequences codes for the same protein as the protein partial sequences, it can not be judged whether or not any example, accession No. R50695) in ESTs, but, since they are of sequences that shared a homology of 90% or more (for sequences of the present cDNA has revealed the registration 15 Furthermore, the search of the GenBank using the base product of high molecular weight.

10 depicts the hydrophobicity/hydrophilicity profile, obtained existed five putative transmembrane domains. Figure 49 protein consisting of 344 amino acid residues and there and a 1092-bp 3'-untranslated region. The ORF codes for a consisting of a 55-bp 5'-untranslated region, a 1035-bp ORF, osteosarcoma cell line Saos-2 revealed the structure 5 insert of clone HP10531 obtained from cDNA library of human Determination of the whole base sequence of the cDNA <HP10531> (SEQ ID Nos. 129, 139, and 149)

of the present invention.

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *D. melanogaster* GOLIATH protein (DM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the *D. melanogaster* GOLIATH protein.

Table 32

HP MGPPGAGVSGRCGGCGGSGRLAMWCFLLALSPQAPGSRGAHAWWATAYLANSWVRPHTGVNR  
 HP TWMELEEGVGQDSLEPVAAGVLVPPDPGALNACNPHHTNFTVPTWGSVQSWMLAL  
 HP QRGGGCTPADKIKHILAYERGASGAVIFNFPFGTRNNEVIMPSPHSGAVDIAIMIGNTKKGKIL

DM ..  
 MQLKMQIKGKTRNINAAVITYQINIGDLS  
 HP QSIQRGIQVTNVIIEVGK---HGPMVNNHYSIFEVSSEFIIITAAATVGYEIFYSAPRLRNA  
 .... \* \* \* \* \*

DM IITLKGYNVTISIIIEGRGVRRTISSLNRTSFLVIS-PIV-DILICWLIFVYIQRFRYM  
 HP HAQSRKQRGLKADAKKAIQRNLQGLTKQGDKEIGPDGDSACAVCIELYKKNDLVHILTCNH  
 ..... \* \* \* \* \*  
 DM QAKDQQRNLCSTVTKKAIIMKIPITKTGKFSQ-EKIDSDSCCAICIEAKKFPPTIRIILPCKH  
 HP IFHKTCVDPWLTLEHNRCTCMCKCDILKALGIEVDVEDGSVSLQVPVSNIEISASASHEEDN  
 \*\*\*\*\* \* \* \* \*

DM EFHKNCIDBPWLTLEHNRCTCMCKCDILKFKFYGVVVGQDIYQTSPPQHTATABISIEIEVPVIVA  
 HP RSEIASSGYASVGQGTDEPPLEEHVQSTNESLQLVNHNHANSVAVDVIPHDNPTFEDEDET  
 DM VPHGQPLQPLQASNMSSAFAPSHYFQSSRSPSSSVQQLAPLTLYQPHHPQOASRGRKNS  
 HP NQETAVREIKS

DM APATMFAHITASHQVTDV

25 Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. A4155685) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

INDUSTRIAL APPLICABILITY



The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarsky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein).

Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished

through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more

preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide, which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides

capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the  
5 table 33 below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 33

Stringency Condition	Poly nucleotide Hybrid	Hybrid Length (bp)	Hybridization Temperature and Buffer <sup>†</sup>	Wash Temperature
A	DNA : DNA	≥50	65°C: 1×SSC -or- 42°C: 1×SSC, 50% formamide	65°C: 0.3×SSC
B	DNA : DNA	<50	T <sub>H</sub> <sup>*</sup> : 1×SSC	T <sub>H</sub> <sup>*</sup> : 1×SSC
C	DNA : RNA	≥50	67°C: 1×SSC -or- 45°C: 1×SSC, 50% formamide	67°C: 0.3×SSC
D	DNA : RNA	<50	T <sub>D</sub> <sup>*</sup> : 1×SSC	T <sub>D</sub> <sup>*</sup> : 1×SSC
E	RNA : RNA	≥50	70°C: 1×SSC -or- 50°C: 1×SSC, 50% formamide	70°C: 0.3×SSC
F	RNA : RNA	<50	T <sub>F</sub> <sup>*</sup> : 1×SSC	T <sub>F</sub> <sup>*</sup> : 1×SSC
G	DNA : DNA	≥50	65°C: 4×SSC -or- 42°C: 4×SSC, 50% formamide	65°C: 1×SSC
H	DNA : DNA	<50	T <sub>H</sub> <sup>*</sup> : 4×SSC	T <sub>H</sub> <sup>*</sup> : 4×SSC
I	DNA : RNA	≥50	67°C: 4×SSC -or- 45°C: 4×SSC, 50% formamide	67°C: 1×SSC
J	DNA : RNA	<50	T <sub>J</sub> <sup>*</sup> : 4×SSC	T <sub>J</sub> <sup>*</sup> : 4×SSC
K	RNA : RNA	≥50	70°C: 4×SSC -or- 50°C: 4×SSC, 50% formamide	67°C: 1×SSC
L	RNA : RNA	<50	T <sub>L</sub> <sup>*</sup> : 2×SSC	T <sub>L</sub> <sup>*</sup> : 2×SSC
M	DNA : DNA	≥50	50°C: 4×SSC -or- 40°C: 6×SSC, 50% formamide	50°C: 2×SSC
N	DNA : DNA	<50	T <sub>N</sub> <sup>*</sup> : 6×SSC	T <sub>N</sub> <sup>*</sup> : 6×SSC
O	DNA : RNA	≥50	55°C: 4×SSC -or- 42°C: 6×SSC, 50% formamide	55°C: 2×SSC
P	DNA : RNA	<50	T <sub>P</sub> <sup>*</sup> : 6×SSC	T <sub>P</sub> <sup>*</sup> : 6×SSC
Q	RNA : RNA	≥50	60°C: 4×SSC -or- 45°C: 6×SSC, 50% formamide	60°C: 2×SSC
R	RNA : RNA	<50	T <sub>R</sub> <sup>*</sup> : 4×SSC	T <sub>R</sub> <sup>*</sup> : 4×SSC

‡ : The hybrid length is that anticipated for the hybridized region(s) of the

hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the

hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

† : SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub> and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after

hybridization is complete.

\*T<sub>H</sub> - T<sub>R</sub> : The hybridization temperature for hybrids anticipated to be less than

10

5

- 50 base pairs in length should be 5-10°C less than the melting temperature ( $T_m$ ) of the hybrid, where  $T_m$  is determined according to the following equations. For hybrids less than 18 base pairs in length,  $T_m(^{\circ}\text{C}) = 2(\# \text{ of A + T bases}) + 4(\# \text{ of G + C bases})$ . For hybrids between 18 and 49 base pairs in length,  $T_m(^{\circ}\text{C}) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\% \text{ G+C}) \cdot (600/N)$ , where N is the number of bases in the hybrid, and  $[\text{Na}^+]$  is the concentration of sodium ions in the hybridization buffer ( $[\text{Na}^+]$  for 1×SSC=0.165M).

- Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

- Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.
2. An isolated DNA coding for the protein according to Claim 1.
3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140.
4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150.
5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eucaryotic cells.
6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.

# CLAIMS



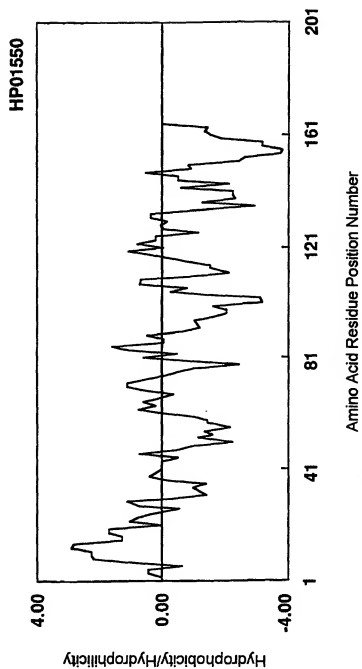


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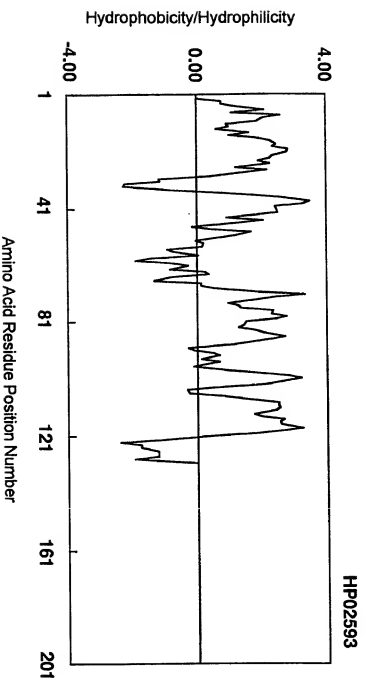


Fig. 2

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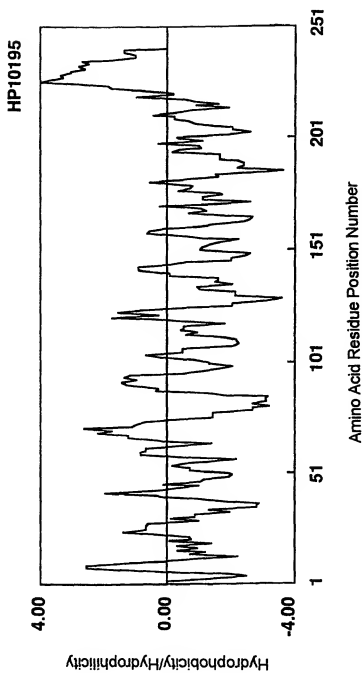


Fig. 3

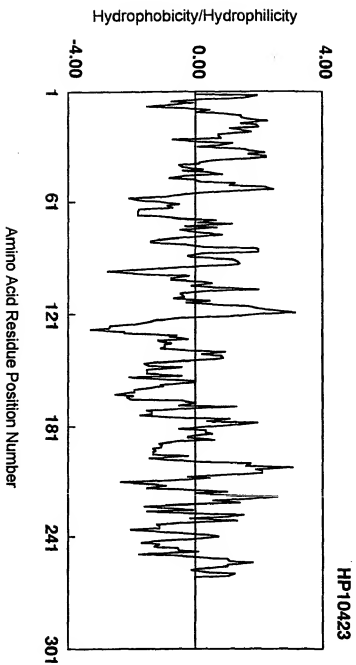


Fig. 4

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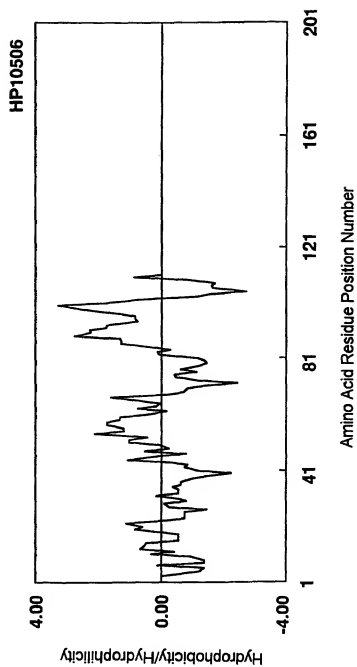


Fig. 5

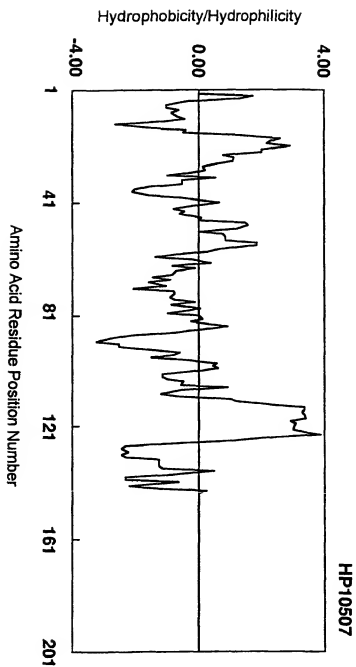


Fig. 6

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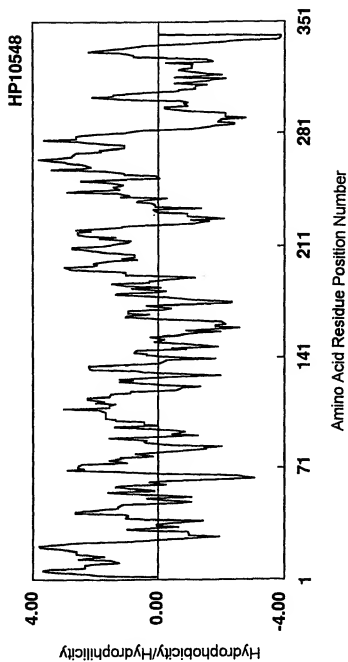


Fig. 7

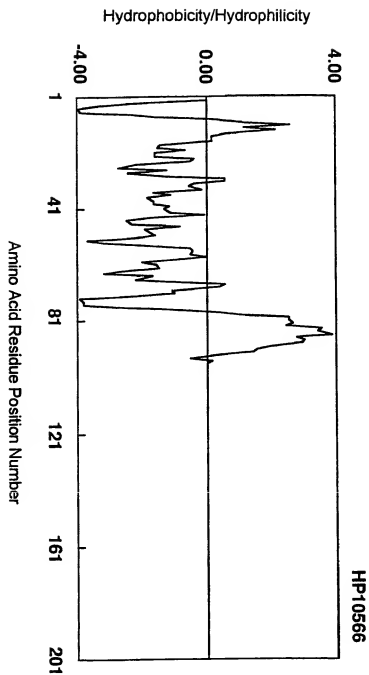


Fig. 8



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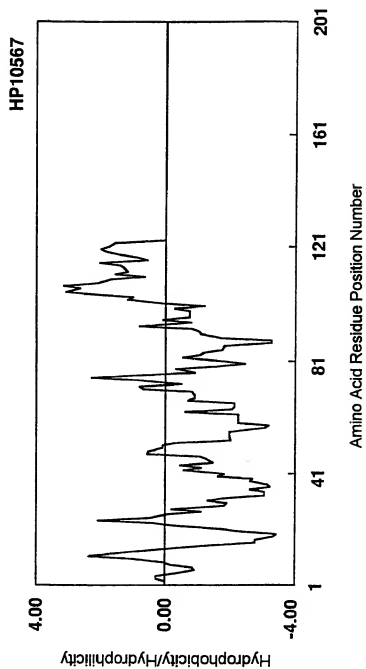


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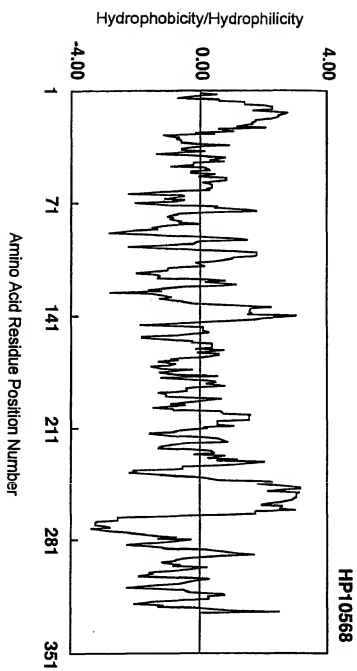


Fig. 10

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WO 00/05367

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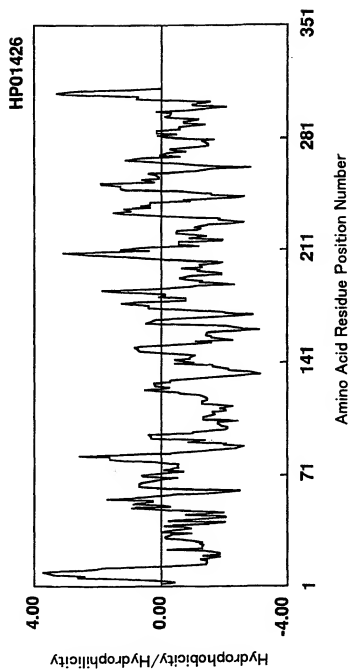


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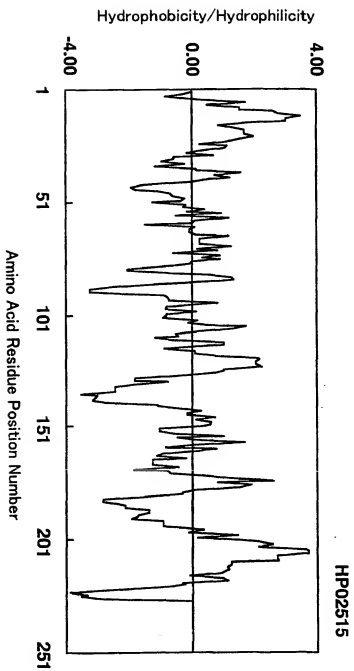


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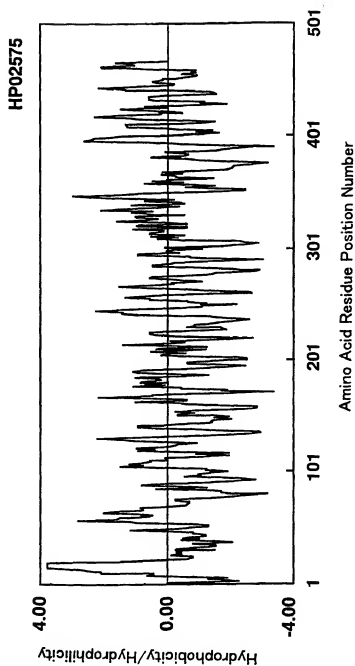


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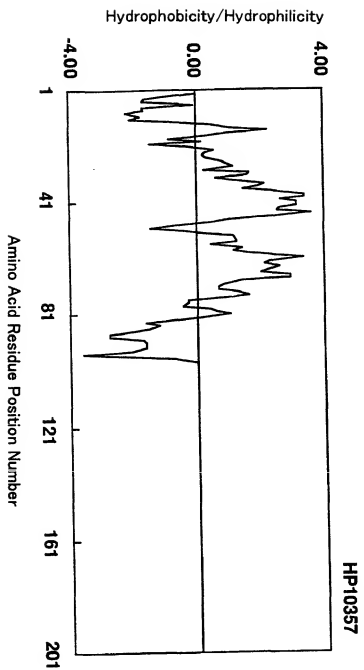


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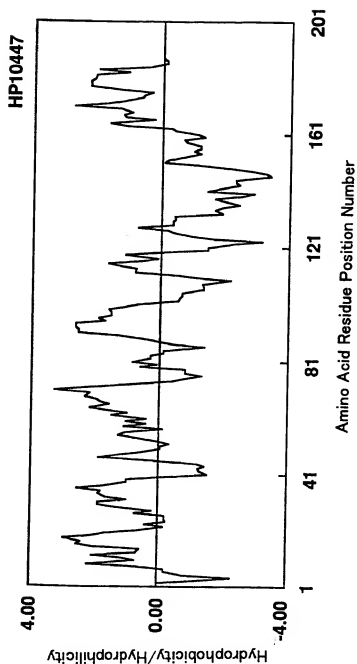


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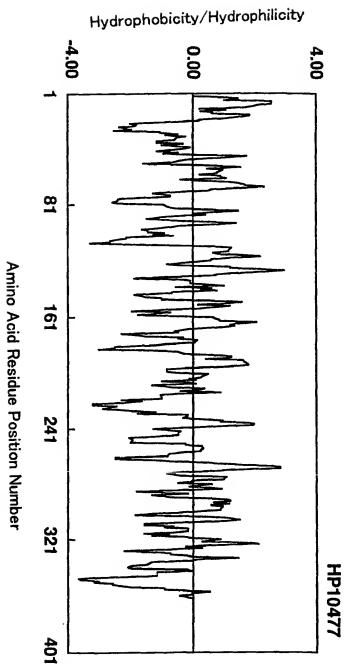


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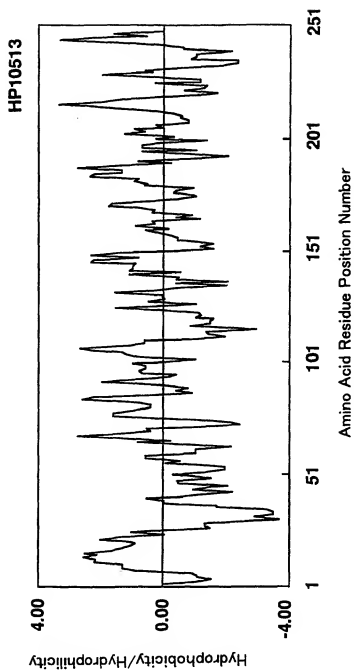


Fig.17

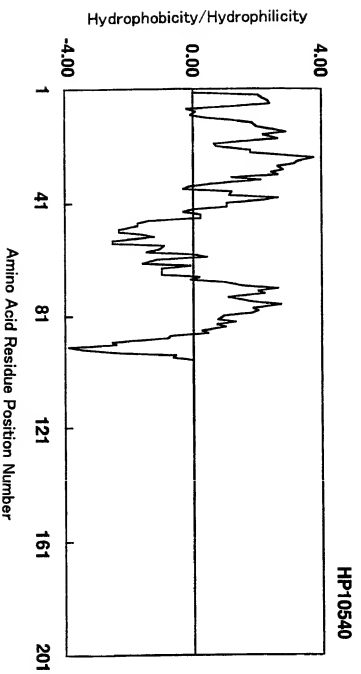


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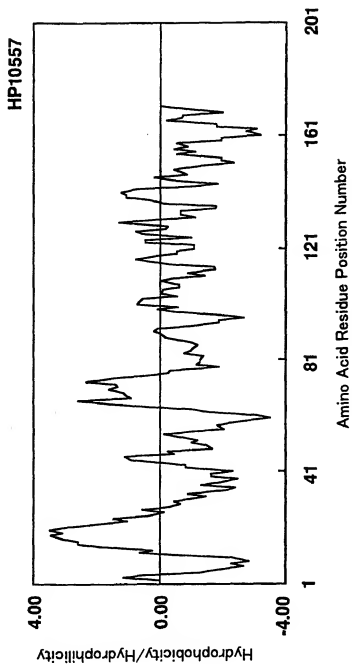


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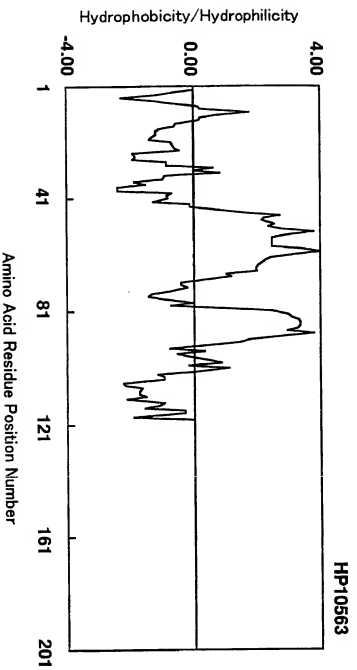


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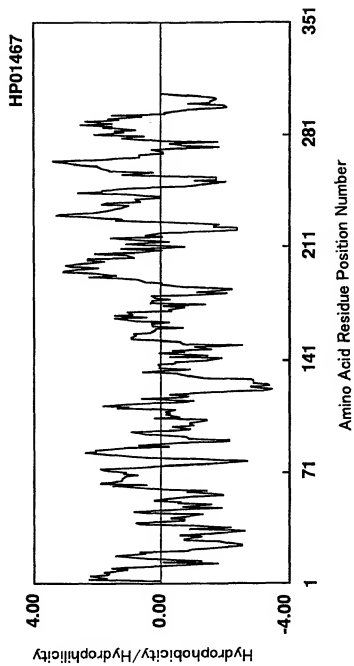


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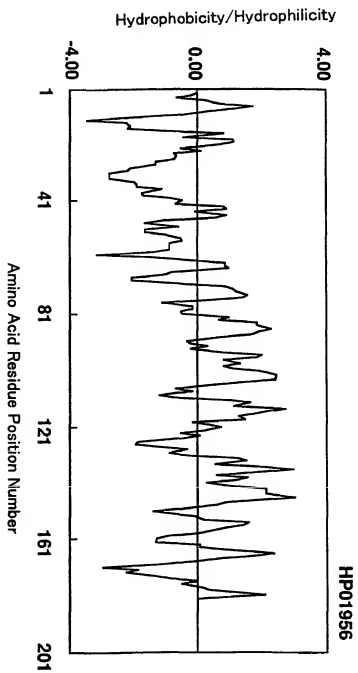


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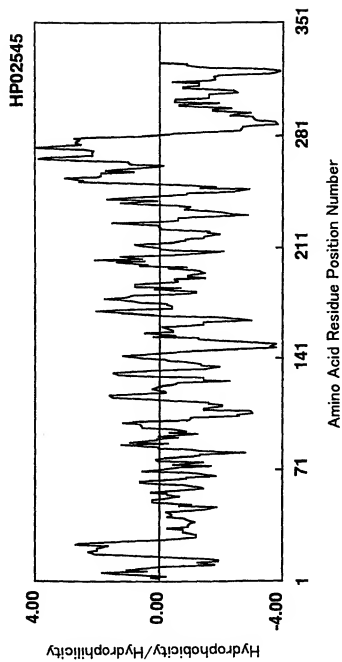


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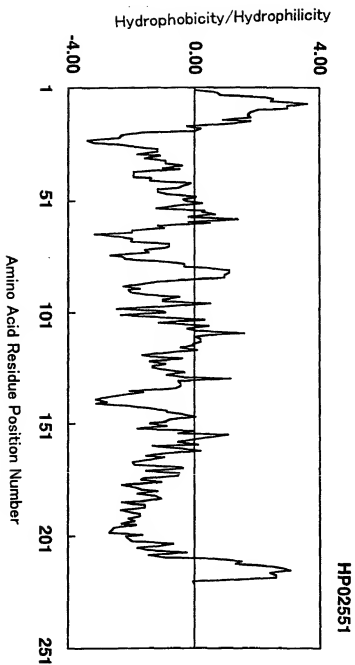


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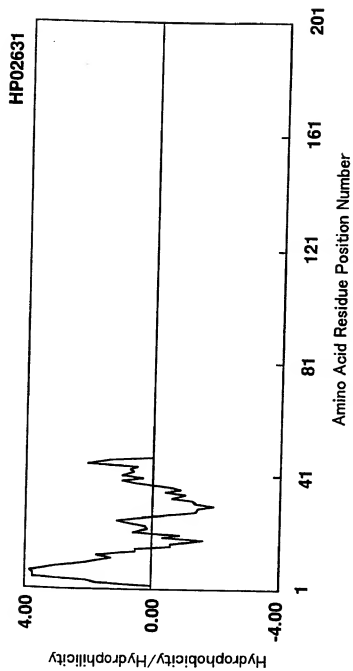


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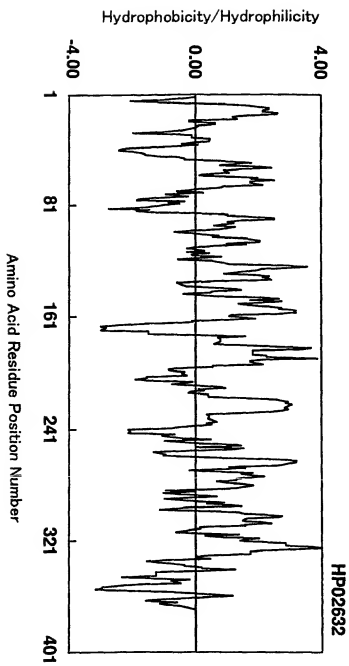


Fig. 26

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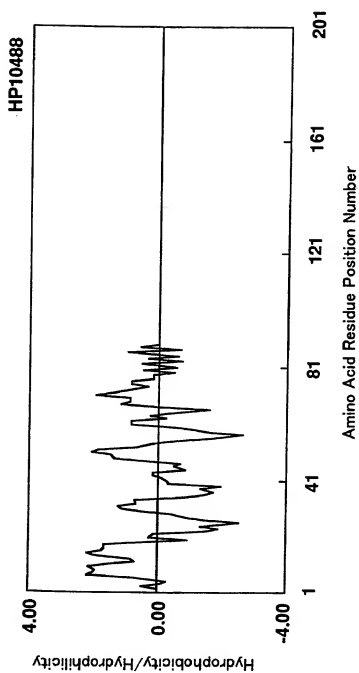


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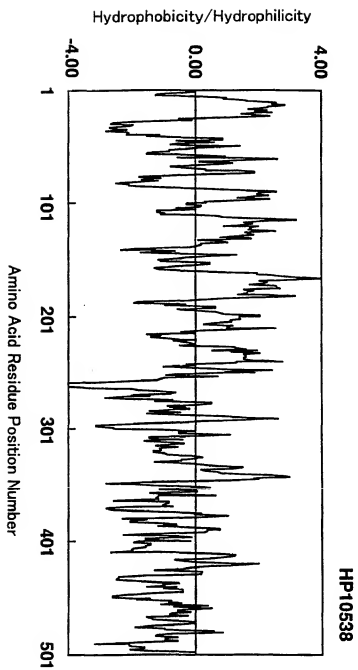


Fig. 28

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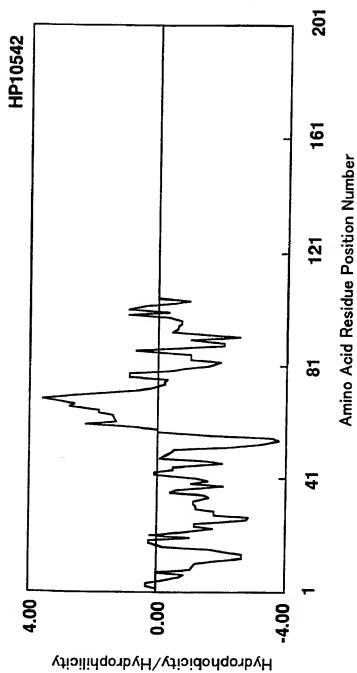


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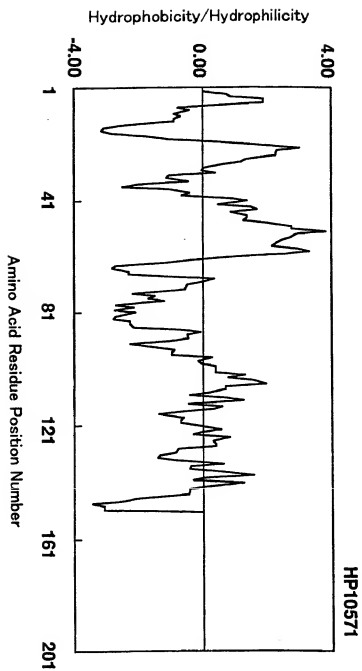


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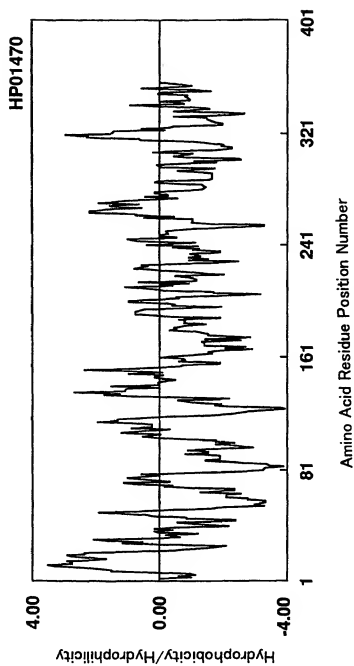


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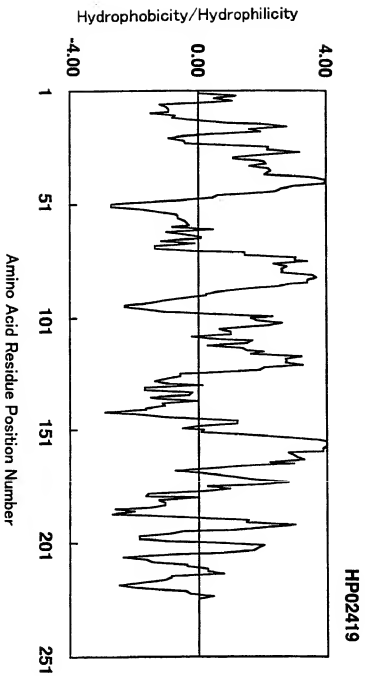


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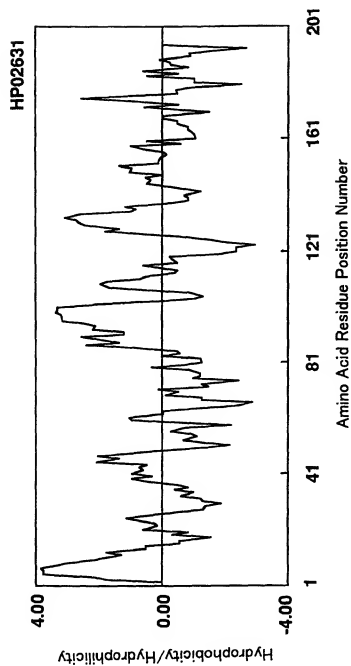


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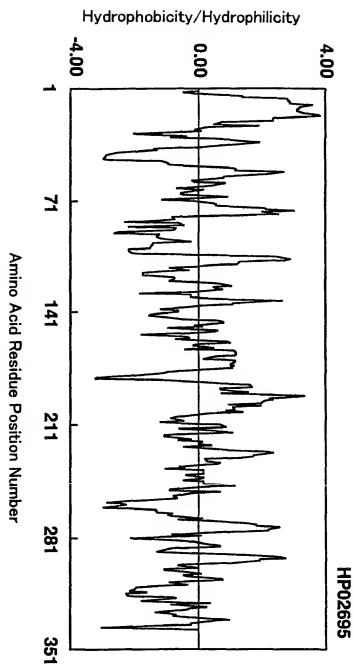


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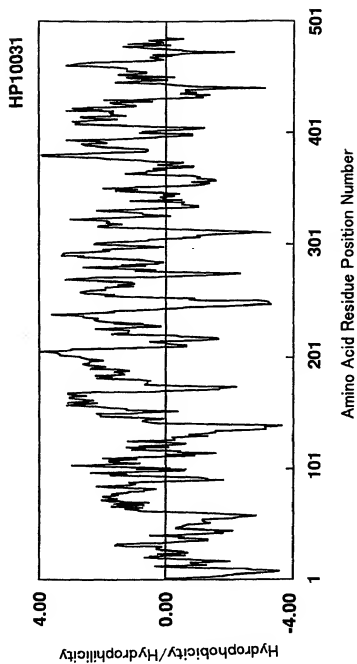


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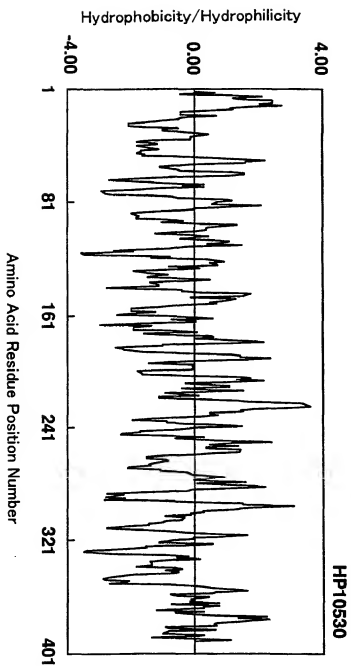


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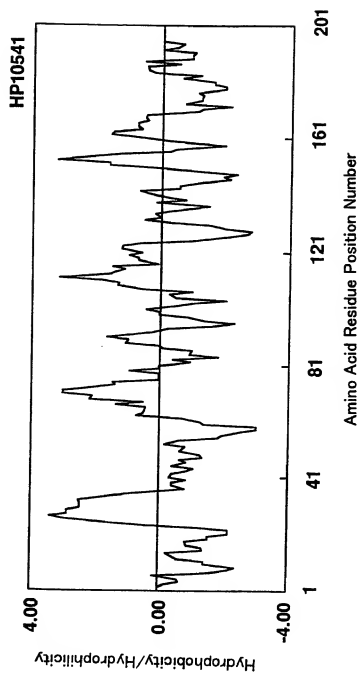


Fig.37

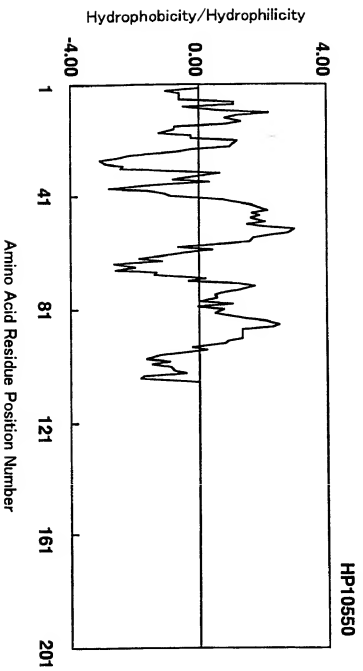


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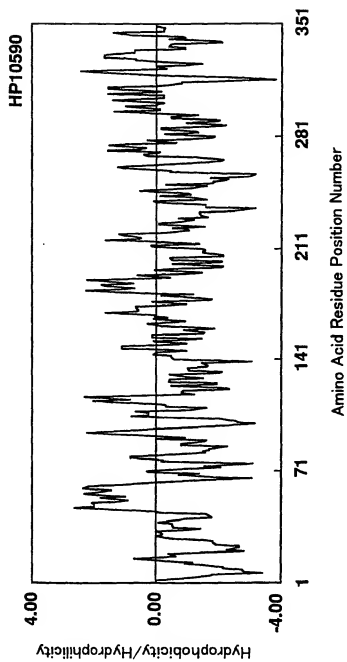


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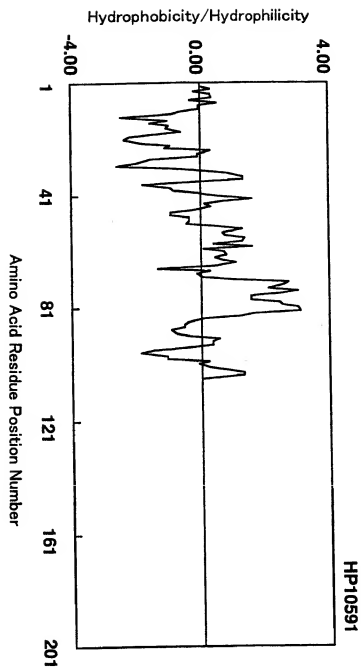


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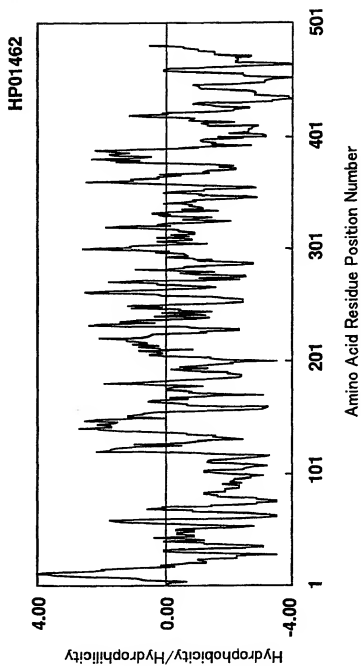


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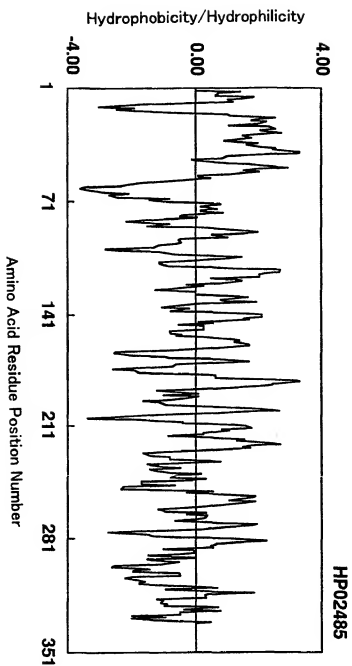


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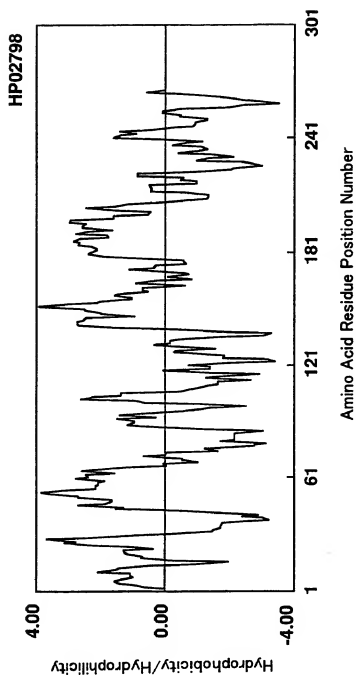


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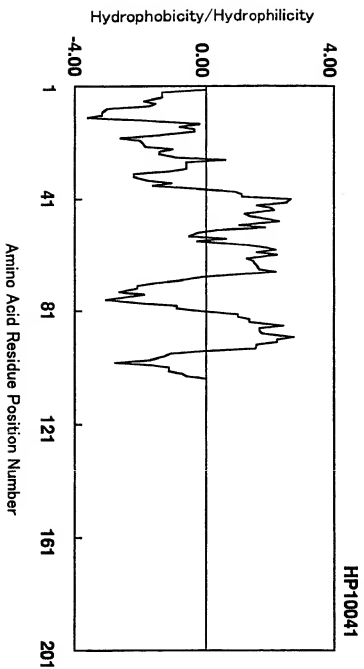


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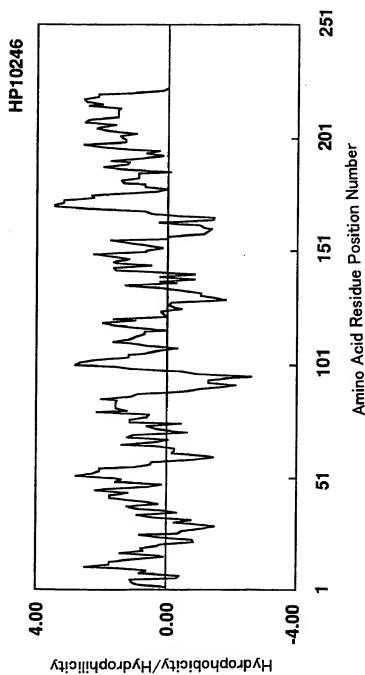


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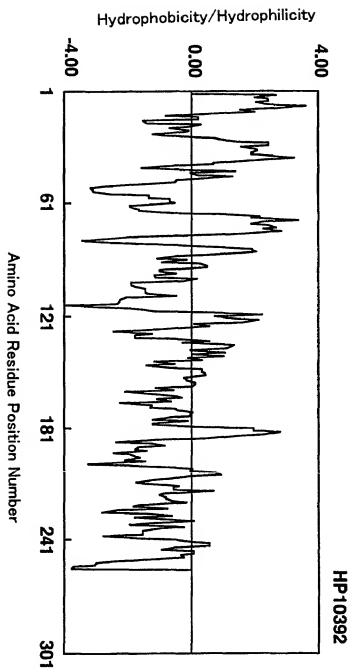


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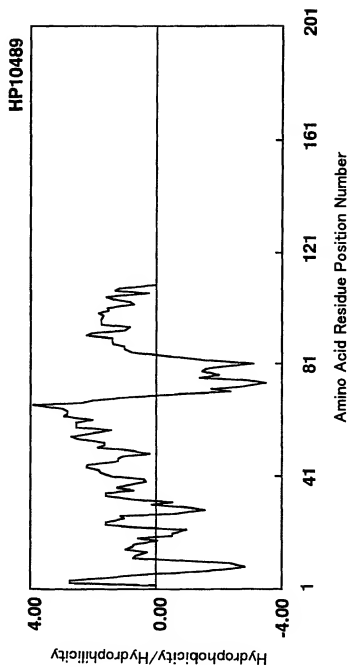


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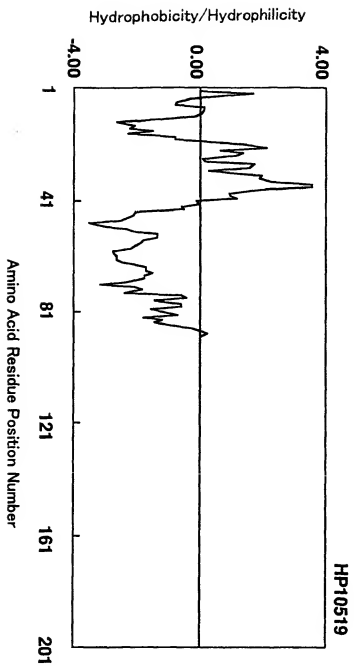


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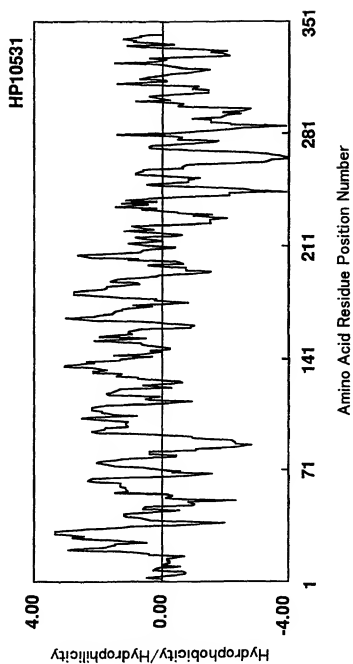


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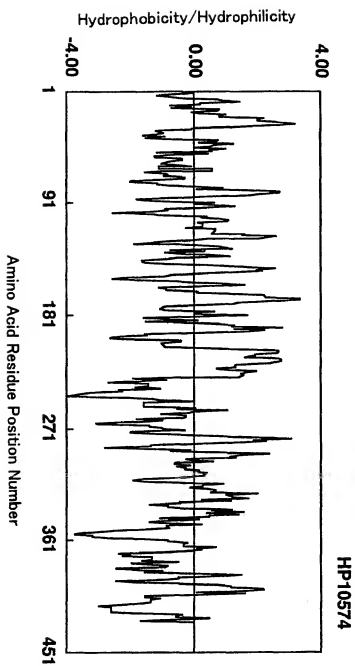


Fig. 50

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	Ala Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Val Met			
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	Ala Ile Val Ser Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp			
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		Asn Ser Arg Leu His Ser Arg Glu Leu Ser Pro Glu Ala Arg Arg Ser	35	40	45
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		Lys Glu Lys Phe Leu Arg Glu Asn Arg Lys Asn Met Leu Leu	65	70	75
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105

110

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115

120

125

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Pro Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly

145

150

155

Ser Thr Ala Leu Arg Cys Ser Ser Gly Ala Pro Lys Pro Val

165

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Tyr Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser

180

185

190

Met Val Gln Asp Gln Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser

195

200

205

Leu Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly

210

215

220

Ser Ala Ser Cys Gln Leu Thr Leu Ser Val Thr Gln Pro Ser Gln Gly

225

230

235

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245

250

255

Ser Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Gln Arg Gly Lys

260

265

270

Lys Pro Lys Gln Thr Tyr Gly Gly Ser Asp Leu Arg Gln Asp Ala Ile

275

280

285

Ala Pro Gly Ile Ser Gln His Thr Cys Met Arg Ala Asp Ser Ser Lys

290

295

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Gly Phe Leu Gln Arg Pro Ser Ser Ala Ser Thr Val Thr Thr Thr Lys

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310

315

Ser Lys Leu Pro Met Val Val

325

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302

350

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b6  
b7C

CONFIDENTIAL

450

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WO 00/05367

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 aag tat aat tca aag cca ttc tgc tgc gaa aaa ctg ctc tcc tgg gtcg aaa  
 Lys Tyr Lys Ser Phe Cys Glu Lys Leu Ser Trp Val Lys  
 100 105 110

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	agc agt ggc tgt gcc aga gtc att gtt ctt tcg agc agt cat tca tat	445
	Ser Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr	
	115 120 125	
	cag cgt aat gat ctg cag ctt cgt agt act ccc ttc cgg tac cta ctt	493
5	Gln Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu	
	130 135 140	
	aca cct tcc atg caa aaa agt gtt caa aat aaa ata aag agc ctt aac	541
	Thr Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn	
	145 150 155	
10	tgg gaa gaa atg gaa aaa agc cgg tgc att cct gaa ata gat gat tcc	589
	Trp Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser	
	160 165 170 175	
	gag ttt tgt atc cgc att ccg gga gga ggt atc aca aaa aca ctc tat	637
	Glu Phe Cys Ile Arg Ile Pro Gly Gly Ile Thr Lys Thr Leu Tyr	
15	180 185 190	
	gat gaa agc tgt tct aaa gaa atc caa atg gca gtt ctg ctg aaa ttt	685
	Asp Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe	
	195 200 205	
	gtt tca gaa ggg gac aac atc cca gat gca tta ggt ctt gtt gag tat	733
20	Val Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr	
	210 215 220	
	ctt aat gag tgg ctt cag ata ctc aaa cca ctt agc gat gac ccc aca	781
	Leu Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr	
	225 230 235	
25	gta tct gcc tca cgg tgg aaa ata cca agt tct tgg aga tta ctc ttt	829
	Val Ser Ala Ser Arg Trp Lys Ile Pro Ser Ser Trp Arg Leu Leu Phe	
	240 245 250 255	
	ggc agt ggt ctt ccc cct gca ctt ttc tgatctaatt tctgttttat acct	880
	Gly Ser Gly Leu Pro Pro Ala Leu Phe	
30	260	
	tatacccaaa acacttacta ccaacacagc tgttaaacat tctatacaaa aaaattgtat	940
	gatctggtat taggaatata ctttcacagt aaatatcaaa gaaaaaagat taagggtctc	1000
	tttgccatgc ttttcacat atgcacaaaa tgtaaatttt gtacaataaa attttatttc	1060
	ctaagt	1066

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17	35	40	45	248
18	50	55	60	296
19	65	70	75	344
20	80	85	90	390
21	95	100	105	450
22	110	115	120	510



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	gtggatacta caagactgag aagaaaatcg tatgttgoa ttctctggct atggagtggt	570
	tgtggccttc acagatttca caggaaacaa taaatccctc agagaagt	618
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	<213> Homo sapiens	
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	cggtcccgcg ccgagggatc ctccacgggg ctatgtggct gcgtcggggg cgggagcggg	120
15	ggtgagcggg cgctaggggc gcgagccccc gccggccctt cctccagcgc cctgcggacc	180
	ccgcagaagg cgctcgccctc cctagccccc aaaaacatat cgatttttct cgctgtggca	240
	acggggagct cctgatagat cctctgctcc aataggcaac tcgggccttc cctgcctga	300
	cctggaaacct ctgggggggc tgcagagtaa gtgcgcctc tgcgctcga cggaggcaag	360
	aggcctgtgg agtaggtccc tctgttcga caggtgcgac acttggcgct cc atg ctt	418
20		Met Leu
		1
	gcg ggt gcc ggg agg cct ggc ctc ccc cag ggc cgc cac ctc tgc tgg	466
	Ala Gly Ala Gly Arg Pro Gly Leu Pro Gln Gly Arg His Leu Cys Trp	
	5 10 15	
25	ttg ctc tgt gct ttc acc tta aag ctc tgc caa gca gag gct ccc gtg	514
	Leu Leu Cys Ala Phe Thr Leu Lys Leu Cys Gln Ala Glu Ala Pro Val	
	20 25 30	
	cag gaa gag aag ctg tca gca agc acc tca aat ttg cca tgc tgg ctg	562
	Gln Glu Glu Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys Trp Leu	
30	35 40 45 50	
	gtg gaa gag ttt gtg gta gca gaa gag tgc tot cca tgc tot aat ttc	610
	Val Glu Glu Phe Val Val Ala Glu Glu Cys Ser Pro Cys Ser Asn Phe	
	55 60 65	
	cgg gct aaa act acc cct gag tgt ggt ccc aca gga tat gta gag aaa	658
35	Arg Ala Lys Thr Thr Pro Glu Cys Gly Pro Thr Gly Tyr Val Glu Lys	

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706	atc aca tgc agc tca tct aag aga aat gag tca aaa agc tgc cgc tca	Ile Thr Cys Ser Ser Ile Arg Asn Glu Phe Lys Ser Cys Arg Ser	85	90	95	754
705	gct tgc atg gaa cga cgc tca tct tgg aag ttc gaa ggc gct gtc gtc	Ala Leu Met Glu Glu Arg Leu Phe Trp Lys Phe Glu Gly Ala Val	100	105	110	754
10	ggt gtc gcc atc ttc gct ctt gtc atc atc cgt cag gaa caa	Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Arg Glu Arg Glu	115	120	125	802
10	tgc gac aga aag gct atg gaa aag gtc cgg aag caa atc gag tcc ata	Leu Asp Arg Lys Ala Leu Glu Lys Val Arg Lys Glu Ile Glu Ser Ile	135	140	145	850
15	taagctaacat ccaaccttgc atccctgggtc ttacagagacc tatctccagac agtgaagtg	aaatggagacat attgcacatc ttgggtctctt ggagaccttgc ggtggagatcc cctttccccc	910	915	920	1021
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30	gtaggcagcgg gtaggcagcgg gtaggcagcgg gtaggcagcgg gtaggcagcgg	gtaggcagcgg gtaggcagcgg gtaggcagcgg gtaggcagcgg gtaggcagcgg	135	140	145	240
35	ttc taa ctc gct tgc gtc atg ggt ctt gtc ctt atc tgc tgc	Met Asp Phe Leu Val Leu Phe Leu	354	360	365	402

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	Phe Tyr Leu Ala Ser Val Leu Met Gly Leu Val Leu Ile Cys Val Cys	
	10 15 20	
	tcg aaa acc cat agc ttg aaa ggc ctg gcc agg gga gga gca cag ata	450
	Ser Lys Thr His Ser Leu Lys Gly Leu Ala Arg Gly Gly Ala Gln Ile	
5	25 30 35 40	
	ttt tcc tgt ata att cca gaa tgt ctt cag aga gcc gtg cat gga ttg	498
	Phe Ser Cys Ile Ile Pro Glu Cys Leu Gln Arg Ala Val His Gly Leu	
	45 50 55	
	ctt cat tac ctt ttc cat acg aga aac cac acc ttc att gtc ctg cac	546
10	Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe Ile Val Leu His	
	60 65 70	
	ctg gtc ttg caa ggg atg gtt tat act gag tac acc tgg gaa gta ttt	594
	Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr Trp Glu Val Phe	
	75 80 85	
15	ggc tac tgt cag gag ctg gag ttg tcc ttg cat tac ctt ctt ctg ccc	642
	Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr Leu Leu Leu Pro	
	90 95 100	
	tat ctg ctg cta ggt gta aac ctg ttt ttt ttc acc ctg act tgt gga	690
	Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Phe Thr Leu Thr Cys Gly	
20	105 110 115 120	
	acc aat cct ggc att ata aca aaa gca aat gaa tta tta ttt ctt cat	738
	Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu Leu Phe Leu His	
	125 130 135	
	gtt tat gaa ttt gat gaa gtg atg ttt cca aag aac gtg agg tgc tot	786
25	Val Tyr Glu Phe Asp Glu Val Met Phe Pro Lys Asn Val Arg Cys Ser	
	140 145 150	
	act tgt gat tta agg aaa cca gct cga tcc aag cac tgc agt gtg tgt	834
	Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Lys His Cys Ser Val Cys	
	155 160 165	
30	aac tgg tgt gtg cac cgt ttc gac cat cac tgt gtt tgg gtg aac aac	882
	Asn Trp Cys Val His Arg Phe Asp His His Cys Val Trp Val Asn Asn	
	170 175 180	
	tgc atc ggg gcc tgg aac atc agg tac ttc ctc atc tac gtc ttg acc	930
	Cys Ile Gly Ala Trp Asn Ile Arg Tyr Phe Leu Ile Tyr Val Leu Thr	
35	185 190 195 200	

978	1074	1170	1218	1266	1314	1362	1420	1432
215	220	225	230	235	240	245	250	255
210	215	220	225	230	235	240	245	250
205	210	215	220	225	230	235	240	245
200	205	210	215	220	225	230	235	240
195	200	205	210	215	220	225	230	235
190	195	200	205	210	215	220	225	230
185	190	195	200	205	210	215	220	225
180	185	190	195	200	205	210	215	220
175	180	185	190	195	200	205	210	215
170	175	180	185	190	195	200	205	210
165	170	175	180	185	190	195	200	205
160	165	170	175	180	185	190	195	200
155	160	165	170	175	180	185	190	195
150	155	160	165	170	175	180	185	190
145	150	155	160	165	170	175	180	185
140	145	150	155	160	165	170	175	180
135	140	145	150	155	160	165	170	175
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115	120	125	130	135	140	145	150	155
110	115	120	125	130	135	140	145	150
105	110	115	120	125	130	135	140	145
100	105	110	115	120	125	130	135	140
95	100	105	110	115	120	125	130	135
90	95	100	105	110	115	120	125	130
85	90	95	100	105	110	115	120	125
80	85	90	95	100	105	110	115	120
75	80	85	90	95	100	105	110	115
70	75	80	85	90	95	100	105	110
65	70	75	80	85	90	95	100	105
60	65	70	75	80	85	90	95	100
55	60	65	70	75	80	85	90	95
50	55	60	65	70	75	80	85	90
45	50	55	60	65	70	75	80	85
40	45	50	55	60	65	70	75	80
35	40	45	50	55	60	65	70	75
30	35	40	45	50	55	60	65	70
25	30	35	40	45	50	55	60	65
20	25	30	35	40	45	50	55	60
15	20	25	30	35	40	45	50	55
10	15	20	25	30	35	40	45	50
5	10	15	20	25	30	35	40	45
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&lt;221&gt; CDS

&lt;222&gt; (62)...(355)

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 c atg act aaa aag aag cgg gag aat ctg ggc gtc gct cta gag atc gat 109  
 Met Thr Lys Lys Lys Arg Glu Asn Leu Gly Val Ala Leu Glu Ile Asp  
 1 5 10 15

ggg cta gag gag aag ctg tcc cag tgt cgg aga gac ctg gag gcc gtg 157  
 10 Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val  
 20 25 30

aac tcc aga ctc cac agc cgg gag ctg agc cca gag gcc agg agg tcc 205  
 Asn Ser Arg Leu His Ser Arg Glu Leu Ser Pro Glu Ala Arg Arg Ser  
 35 40 45

15 ctg gag aag gag aaa aac agc cta atg aac aaa gcc tcc aac tac gag 253  
 Leu Glu Lys Glu Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Glu  
 50 55 60

aag gaa ctg aag ttt ctt cgg caa gag aac cgg aag aac atg ctg ctc 301  
 Lys Glu Leu Lys Phe Leu Arg Gln Glu Asn Arg Lys Asn Met Leu Leu  
 20 65 70 75 80

tct gtg gcc atc ttt atc ctc ctg acg ctc gtc tat gcc tac tgg acc 349  
 Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr  
 85 90 95

atg tgagcctggc acttccccc aaccagcaca ggcttccact tggccccc 400  
 25 Met

tgatcaggat caagcaggca cttcaagcct caataggacc aagggtctgg ggtgttcccc 460  
 tcccaacctta gtgtcaagc atggcttccct ggcggccacc gccttgccct cctggcctgc 520  
 tgggggggttc cgggtctcca gaaggacatg gtgctgtgcc ctccottage ccaagggaga 580  
 30 ggcaataaag acacaagct g 601

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&lt;211&gt; 585

&lt;212&gt; DNA

35 &lt;213&gt; Homo sapiens

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၀၇၂            ဘုရားသခင်တို့၏အမည်များကို အောက်ပါအတိုင်း ရေးသားဖော်ပြပါ။

၀၈            မိမိတို့အတွက် အကျိုးရှိစေမည့် ဆရာတစ်ပါး၏အမည်ကို ရေးသားဖော်ပြပါ။

gac tcc ccc asp tyr phe	30	asp tyr phe asn lys gly	35	gag gcc gaa pro gln asp	40	gag ccc gaa asp tyr phe	45	gag ccc gaa asp tyr phe	50	trp gln ile trp gln ile	55	met lys ser asn gln asp	254
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[illegible][illegible]

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 15 Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly Phe Leu  
5 10 15  
 tgc ctg agt ggg ctg gcc gtg gag gtg aag gta ccc aca gag ccg ctg 155  
 Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro Leu  
20 25 30  
 20 agc acg ccc ctg ggg aag aca gcc gag ctg acc tgc acc tac agc acg 203  
 Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser Thr  
35 40 45  
 tgc gtg gga gac agc ttc gcc ctg gag tgg agc ttt gtg cag cct ggg 251  
 Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro Gly  
 25 50 55 60 65  
 aaa ccc atc tct gag tcc cat cca atc ctg tac ttc acc aat ggc cat 299  
 Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly His  
70 75 80  
 ctg tat cca act ggt tct aag tca aag cgg gtc agc ctg ctt cag aac 347  
 30 Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln Asn  
85 90 95  
 ccc ccc aca gtg ggg gtg gcc aca ctg aaa ctg act gac gtc cac ccc 395  
 Pro Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His Pro  
100 105 110  
 35 tca gat act gga acc tac ctc tgc caa gtc aac aac cca cca gat ttc 443

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	ser asp thr gly thr tyr leu cys gln val asn asn pro pro asp phe	115	120	125	491
	tac acc aat gag tgg ctg ggg cta atc aac ctt act gtc ctg gtt ccc ccc	130	135	140	491
5	tyr thr asn gly leu gly leu ile asn leu thr val leu val pro pro	145	150	155	539
	ser asn pro leu cys ser gln ser gly gln thr ser val gly ser	160	165	170	539
10	thr ala leu arg cys ser ser gln gly ala pro lys pro val tyr	175	180	185	587
	aac tgg gtc ggt cgt ctt gga act ttt cct aca cct tct cct ggc agc atg	190	195	200	635
	asn trp val arg leu gly thr phe pro thr pro ser pro gly ser met	205	210	215	683
15	glt caa gat gag gtc tcc ggc cag ctc att ctc aac ctc tcc ctg	220	225	230	
	val gln asp gln val ser gly gln leu ile leu thr asn leu ser leu	235	240	245	
	acc tcc tcc ggc acc tac cgc tgt gtc ggc acc aac cag atg ggc agt	250	255	260	731
20	thr ser ser gly thr tyr arg cys val ala thr asn gln met gly ser	265	270	275	779
	gaa tcc tcc gtc gag ctc tcc tct gtc aac gaa ccc tcc caa ggc cga	280	285	290	
	ala ser cys gln leu thr leu ser val thr gln pro ser gln arg	295	300	305	
25	gtg gcc gga gct ctg atc ggg gtc ctc ctg ggc gtc ctg ctg cta	310	315	320	827
	val ala gly ala leu ile gly val leu leu gly val leu leu ser	325	330	335	
	glt gct gct ggc ttc tgc ctg gtc acc gaa gag agg ggg aag aag	340	345	350	875
	val ala ala phe cys leu val arg phe gln lys gln arg gly lys lys	355	360	365	923
30	ccc aag gag aca tat ggg ggt agt gac ctc cgg gag gat gcc atc gct	370	375	380	971
	pro lys gln thr tyr gly ser asp leu arg gln asp ala ile ala	385	390	395	
35	cct ggg atc tct gag caa act tgt atg agg gct gat tct aac gag ggy	400	405	410	
	pro gly ile ser gln his thr cys met arg ala asp ser ser lys gly	415	420	425	



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ttc ctg gaa aga ccc tgg tct gcc agc acc gtg acg acc acc aag tcc      1019
Phe Leu Glu Arg Pro Ser Ser Ala Ser Thr Val Thr Thr Thr Lys Ser
          310                      315                      320

aag ctc cct atg gtc tgactctccc cgatccctga gggcggtgag ggg      1070
5  Lys Leu Pro Met Val Val
          325

gaatatcaat aattaaagtc tgtgggtacc      1100

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    <213> Homo sapiens

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    Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser
          20          25          30
    Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys
20          35          40          45
    Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val
    50          55          60
    Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr
    65          70          75          80
25 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val
          85          90          95
    Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu
          100          105          110
    Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala
30          115          120          125
    Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala
    130          135          140
    Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His
    145          150          155          160
35 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu

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175	Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Ala Ala	170		165	
190	Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val	185		180	
195	Lys Tyr Gly Gln Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro	200		195	
210	Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser	215		210	
225	Pro Tyr Gly Gln Arg Gln Phe Thr Ala Gly Phe Val Gln Phe Arg Val	230		225	
240	Phe Asn Asn Gln Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val	250		245	
255	Thr Gly Cys Asn Thr Gln His His Cys Ile Gly Gly Gly Tyr Phe	265		260	
270	Pro Gln Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp	285		275	
280	Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Gln Ile Thr	295		290	
300	Gln Ala Ala Val Leu Leu Phe Tyr Arg	310		305	
320	<210> 32				
325	<211> 229				
330	<212> PRT				
335	<213> Homo sapiens				
340	<400> 32				
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355	Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu	360		20	
365	Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Cys Phe	370		35	
375	Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Gln Ile Gln Tyr Gln Val	380		50	
385	Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Gln	390		55	
		60			

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65                      70                      75                      80  
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr  
                                  85                      90                      95  
 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe  
 5                      100                      105                      110  
 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn  
                                  115                      120                      125  
 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr  
                                  130                      135                      140  
 10 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile  
                                  145                      150                      155                      160  
 Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu  
                                  165                      170                      175  
 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe  
 15                      180                      185                      190  
 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val  
                                  195                      200                      205  
 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys  
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 20 Arg Lys Ser Arg Thr  
                                  225  
  
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                                  <213> Homo sapiens  
  
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 Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr  
                                  20                      25                      30  
 Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala  
                                  35                      40                      45  
 35 Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe

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5	65	Ser Val Pro Ser Phe Gly Ser Gln Trp Phe Trp Tyr Trp Gln Lys	55	60
	80			
	95	Gln Lys Ile Pro Lys Tyr Val Gln Phe Met Lys Asp Asn Tyr Pro		
5	85	Ser Phe Lys Tyr Gln Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe	90	
	100			
	110	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	105	
	115			
10	120	Ile Val Leu Thr Ser Lys His Gln Gly Phe Thr Leu Trp Gly Ser	125	
	130			
	135	Gln Tyr Ser Trp Asn Trp Asn Ala Ile Asp Gln Gly Pro Lys Arg Asp	140	
	145			
	150	Ile Val Lys Gln Leu Gln Val Ala Ile Arg Asn Arg Thr Asp Leu Arg	155	
15	165	Phe Gly Leu Tyr Ser Leu Phe Gln Trp Phe His Pro Leu Phe Leu	170	
	180			
	185	Gln Asp Gln Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys	190	
	195			
20	200	Thr Leu Pro Gln Leu Tyr Gln Leu Val Asn Asn Tyr Gln Pro Gln Val	205	
	210			
	215	Leu Trp Ser Asp Gly Asp Gly Ala Pro Asp Gln Tyr Trp Asn Ser	220	
	225			
	230	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Gln Ser Pro Val Arg Gly Thr	235	
25	245	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly	250	
	255			
	260	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro	265	
	275			
30	280	His Lys Trp Gln Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr	285	
	290			
	295	Arg Arg Gln Ala Gly Ile Ser Asp Tyr Leu Thr Ile Gln Leu Val	300	
	305			
	310	Lys Gln Leu Val Gln Thr Val Ser Cys Gly Gln Asn Leu Leu Met Asn	315	
35	325			
	330			
	335			

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Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg  
 340 345 350

Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr  
 355 360 365

5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val  
 370 375 380

Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu  
 385 390 395 400

Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile  
 10 405 410 415

Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn  
 420 425 430

Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu  
 435 440 445

15 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr  
 450 455 460

Asn Val Ile  
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20 <210> 34  
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 <212> PRT  
 <213> Homo sapiens

25 <400> 34  
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 1 5 10 15

Val Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu  
 20 25 30

30 Val Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro  
 35 40 45

Glu Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr  
 50 55 60

Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu  
 35 65 70 75 80

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phe Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Gln Lys Lys  
95 90 85  
Glu Val Leu

5 <210> 35

<211> 189

<212> PRT

<213> Homo sapiens

10

<400> 35

Met Cys Gln Gly Gly Asn Leu Gly Gly Ile Lys Met Val His Leu

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Leu Val Leu Ser Gly Ala Trp Gly Met Gln Met Trp Val Thr Phe Val

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Ser Gly Phe Leu Phe Arg Ser Leu Pro Arg His Thr Phe Gly Leu

35 40 45

Val Gln Ser Lys Leu Phe Pro Phe Tyr Phe His Ile Ser Met Gly Cys

50 55 60

Ala Phe Ile Asn Leu Cys Ile Leu Ala Ser Gln His Ala Trp Ala Gln

65 70 75 80

Leu Thr Phe Trp Gln Ala Ser Gln Leu Tyr Leu Phe Leu Ser Leu

85 90 95

Thr Leu Ala Thr Val Asn Ala Arg Trp Leu Gln Pro Arg Thr Thr Ala

100 105 110

Ala Met Trp Ala Leu Gln Thr Val Gln Lys Gln Arg Gly Leu Gly Gly

115 120 125

Glu Val Pro Gly Ser His Gln Gly Pro Asp Pro Tyr Arg Gln Leu Arg

130 135 140

Glu Lys Asp Pro Lys Tyr Ser Ala Leu Arg Gln Asn Phe Thr Arg Tyr

145 150 155 160

His Gly Leu Ser Ser Leu Cys Asn Leu Gly Cys Val Leu Ser Asn Gly

165 170 175

Leu Cys Leu Ala Gly Leu Ala Leu Gln Ile Arg Ser Leu

180 185

35

30

25

20

15

10

5

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<210> 36  
 <211> 363  
 <212> PRT  
 <213> Homo sapiens

5

&lt;400&gt; 36

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 1 5 10 15  
 Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr  
 10 20 25 30  
 Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu  
 35 40 45  
 Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu  
 50 55 60  
 15 Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Glu Pro Arg  
 65 70 75 80  
 Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala  
 85 90 95  
 Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala  
 100 105 110  
 20 Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val  
 115 120 125  
 Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Gln Cys Met Ser  
 130 135 140  
 25 Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr  
 145 150 155 160  
 Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly  
 165 170 175  
 Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly  
 180 185 190  
 30 Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp  
 195 200 205  
 Phe Thr Arg Cys Ala Ala Asn Met Arg Ser Met Gln Arg Tyr His Gln  
 210 215 220  
 35 Asp Thr Gln Gly Trp Gly Asp Ile Gly Tyr Ser Phe Val Val Gly Ser

225	230	235	240	245	250	255	260	265	270	275	280	285	290	295	300	305	310	315	320	325	330	335	340	345	350	355	360	365	370	375	380	385	390	395	400	405	410	415	420	425	430	435	440	445	450	455	460	465	470	475	480	485	490	495	500	505	510	515	520	525	530	535	540	545	550	555	560	565	570	575	580	585	590	595	600	605	610	615	620	625	630	635	640	645	650	655	660	665	670	675	680	685	690	695	700	705	710	715	720	725	730	735	740	745	750	755	760	765	770	775	780	785	790	795	800	805	810	815	820	825	830	835	840	845	850	855	860	865	870	875	880	885	890	895	900	905	910	915	920	925	930	935	940	945	950	955	960	965	970	975	980	985	990	995	1000
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	------



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				85				90					95			
	Ala	Ile	Ile	Arg	Glu	Leu	Gly	Gly	Ile	Pro	Ile	Val	Ala	Asn	Lys	Ile
				100					105					110		
	Asn	His	Ser	Asn	Gln	Ser	Ile	Lys	Glu	Lys	Ala	Leu	Asn	Ala	Leu	Asn
5				115					120					125		
	Asn	Leu	Ser	Val	Asn	Val	Glu	Asn	Gln	Ile	Lys	Ile	Lys	Val	Gln	Val
				130					135					140		
	Leu	Lys	Leu	Leu	Leu	Asn	Leu	Ser	Glu	Asn	Pro	Ala	Met	Thr	Glu	Gly
				145					150					155		160
10	Leu	Leu	Arg	Ala	Gln	Val	Asp	Ser	Ser	Phe	Leu	Ser	Leu	Tyr	Asp	Ser
					165						170				175	
	His	Val	Ala	Lys	Glu	Ile	Leu	Leu	Arg	Val	Leu	Thr	Leu	Phe	Gln	Asn
				180						185					190	
	Ile	Lys	Asn	Cys	Leu	Lys	Ile	Glu	Gly	His	Leu	Ala	Val	Gln	Pro	Thr
15				195					200					205		
	Phe	Thr	Glu	Gly	Ser	Leu	Phe	Phe	Leu	Leu	His	Gly	Glu	Glu	Cys	Ala
				210					215					220		
	Gln	Lys	Ile	Arg	Ala	Leu	Val	Asp	His	His	Asp	Ala	Glu	Val	Lys	Glu
				225				230				235				240
20	Lys	Val	Val	Thr	Ile	Ile	Pro	Lys	Ile							
					245											
	<210>			38												
	<211>			98												
25	<212>			PRT												
	<213>			Homo sapiens												
	<400>			38												
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30		1			5					10					15	
	Val	Leu	Ser	Ala	Trp	Gly	Val	Ile	Met	Leu	Ile	Met	Leu	Gly	Ile	Phe
				20						25					30	
	Phe	Asn	Val	His	Ser	Ala	Val	Leu	Ile	Glu	Asp	Val	Pro	Phe	Thr	Glu
				35						40					45	
35	Lys	Asp	Phe	Glu	Asn	Gly	Pro	Gln	Asn	Ile	Tyr	Asn	Leu	Tyr	Glu	Gln

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5	Val Arg	50	55	60	65	70	75	80	85	90	95
	Val Ser Tyr Asn Cys Phe Ile Ala Gly Leu Tyr Leu Ileu Gly										
	Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Gln Tyr Met										
5			85	90							
10	<210> 39										
	<211> 172										
	<212> PRT										
	<213> Homo sapiens										
15	Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu	1	5	10	15						
	Ala Leu Val Ileu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly	20	25	30							
	Gln Thr Pro Arg Pro Ala Gln Arg Gly Pro Pro Val Arg Leu Phe Thr	35	40	45							
20	Gln Gln Ileu Ala Arg Tyr Gly Gln Gln Asp Gln Pro Ile	50	55	60							
	Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Gln	65	70	75	80						
	Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser	85	90	95							
25	Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His	100	105	110							
	Asp Thr Thr Gly Leu Thr Ala Lys Gln Ileu Gln Ala Leu Asp Gln Val	115	120	125							
30	Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala	130	135	140							
	Arg Arg Ile Leu Asn Gln Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro	145	150	155	160						
35	Gln Asp Gln Pro His Phe Asp Ile Lys Asp Gln Phe	165	170								

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<210> 40  
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 5 <213> Homo sapiens  
  
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 10 Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile Asp Leu  
 20 25 30  
 Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile Ala Leu  
 35 40 45  
 Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Gly Ser  
 15 50 55 60  
 Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg Ala Val  
 65 70 75 80  
 Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe Tyr His  
 85 90 95  
 20 Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr Ser Tyr  
 100 105 110  
 Asp Asp Ile Pro Asp Phe Asp Asp  
 115 120  
  
 25 <210> 41  
 <211> 939  
 <212> DNA  
 <213> Homo sapiens  
  
 30 <400> 41  
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 gaggctaata ctacttcaa ggaatggacc tgttcttcgt ctccatctct gccacagaagc 120  
 tgcaaggaaa tcaagacga atgtcctagt gcatttgatg gccgtgattt tctcgcact 180  
 gagaatgggtg ttatctacca gaccttctgt gacatgacct ctgggggtgg cggtcggacc 240  
 35 ctggtggcca gcgtgcata gaatgacatg cgtgggaagt gcacggtggg cgatcgctgg 300



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	<400> 43	
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	ctgcgcgcgc cgcgcgtgcc tgcaccacag gccacgcgct togaccocac ctgggagctc	120
5	ctggacgcgc gccagctgcc cgcgtggttt gaccaggcca agttcggcac ctccatccac	180
	tggggagtggt ttccgtgcc cagcttcggt agcagagtggt tctggtggta ttggcaaaag	240
	gaaaagatac cgaagtatgt ggaatttatg aaagataatt accctcctag ttccaaatat	300
	gaagattttg gaccactatt tacagcaaaa ttttttaatg ccaaccagtg ggcagatat	360
	tttcaggcct ctggtgccaa atacattgtc ttaacttcca aacatcatga aggctttaac	420
10	ttgtgggggt cagaatatcc gtggaactgg aatgccatag atgaggggccc caagagggac	480
	attgtcaagg aacttgaggt agccattagg aacagaactg acctgcgttt tggactgtac	540
	tattcccttt ttgaatgggt tcatccgctc ttcccttgagg atgaatccag ttcattccat	600
	aagcggcaat ttccagtttc taagacattg ccagagctct atgagttagt gaacaactat	660
	cagcctgagg ttctctgggc ggatggtagc ggaggagcac cggatcaata ctggaacagc	720
15	acagctctct tggcctggtt atataatgaa agccagttc ggggcacagt agtcaccaat	780
	gatcgttggg gagctggtag catctgtaag catggtggct tctatacctg cagtgatcgt	840
	tataaccoag gacatctttt gccacataaa tgggaaaaact gcatgacaat agcaaaaactg	900
	tcctggggct ataggaggga agctggaatc tctgactatc ttacaattga agaattggtg	960
	aagcaacttg tagagacagt ttcattgtga ggaatcttt tgatgaatat tgggcccaca	1020
20	ctagatggca ccattctgt agtttttgag gagcgactga ggcnaatggg gctcctggcta	1080
	aaagtcacat gagaaactat ttatgaaacc catacctggc gatccacaga tgacactgtc	1140
	accccagatg tgtggtacac atccaaacct aaagaaaaat tagctctatgc cattttctct	1200
	aatggccca catcaggaca gctgttccct ggccatccca aagctattct gggggcaaca	1260
	gaggtgaac tactgggcca tggacagcca cttaactgga ttcttttggg gcaaaatggc	1320
25	attatggtag aactgccaca gctaaccatt catcagatgc cgtgtaaatg gggctgggct	1380
	ctagccctga ctaattgtgat c	1401
	<210> 44	
	<211> 297	
30	<212> DNA	
	<213> Homo sapiens	
	<400> 44	
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35	gtgaagatgc tgcggctgga tattatcaac tcactggtaa caacagtatt catgctcatc	120

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gltcactgtgtc tgcagccatgat accagagaaacc accaacatcga cagtttgtgtgt agtgtgtgtc 180  
 gtaactctga caagatgtatg ctgtctctgcg gaagtggtacc ttaattaccg gaaagcttcg 240  
 ttcaatccca gctgtctcta caagcagaaag ctgtgtgcata aaaaaaaaga agttctg 297

5

&lt;210&gt; 45

&lt;211&gt; 567

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

10

&lt;400&gt; 45

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 ggtgacctgtgt gaaatgcgaat gtggtgtgaac tctgctcag gcttccatgct ttctccagaaag 120  
 cttccaccagc ataaccttcag ataaccttcag agctaaatcct tccacctctca cttccaaatcc 180  
 tcaatgtgtgt gtgctctcat caaacctctgc atctctgtgtc ttaggtctcag 240  
 ctcaaatctc ggtgaggtccag caagctcttca ctgtctgttcc gcttggaccatc 300  
 gtcaaacgccgc gctgtcttga aaccaccgcaacc acaagcttgcac tgttgggccctc gtaaacacctgt 360  
 gaaagagagag gaaagacctgt tgggtgtgtga ccaaggtcaagc accaaggtctcc cgaatccctaac 420  
 ccgcaagctgac gaaagaaagaa acccaaaatca agtgatctccac gccaagaaatct cttctccatac 480  
 caatgtgtgtct cctctctcttg caatctctgtgc tggctctcctga gcaatgtgtct ctgtctcctc 540  
 ggtcctctgcac tggaaatcaag gaagctctc 567

20

&lt;210&gt; 46

&lt;211&gt; 1089

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

25

&lt;400&gt; 46

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 ggtctcccaaga cccaagaaatcga tccaagaaatcga ggaatctgaag gctgtctgga ccaagctctct 120  
 gctccctcagca cctctcagctat tcttggaaaccc aaggtcaatctc tgtctaaacaa ggtctctctcc 180  
 aatctgggaccacc tggatctcttga gaaatcaacctga gctcggaaatcc tgaagctccagc tgaagctccaggg 300  
 ccaatccctccca gccaacctgtgc gaaacctcagc ggtgtgtgtctg aatctcagctccag aagaaaccaaggg 360  
 tctccgctcagca aatctccagctg gcaaaacaggtc gctcgtctctcga cttccagagctcc cactccctctgccc 420  
 caagaaagctga gctggaagaaac gctcgaagaaac gctcgaagaaac gctcgaagaaac gctcgaagaaac 480

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gaggccttcc tgggatgccc ggccatccac ccccgctgcc gctggggagc ggcgcttat 540  
 cggggccgcc cgaagctget gcagctgccg ctgggattct tgtacgtgca teacacctac 600  
 gtgcctgcac caccctgcac ggacttcacg cgtgcgagc ccaacatgcg ctccatgcag 660  
 cgctaccacc aggacacgca aggctgggga gacatcggtc acagtttctg ggtgggctcg 720  
 5 gacggctacg tgtacgaggg acgcggctgg cactgggtgg gcgcccacac gctcggccac 780  
 aactccgggg gcttcggcgt ggccatagtg ggcaactaca ccgcgcgctt gccacgcag 840  
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 gacctccaa 1089

&lt;210&gt; 47

&lt;211&gt; 747

15 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

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 20 tgcactgca ttacaggct gaccggggt cggcgggggg gcgaccgcga gctcgggata 120  
 cgctcttcga agtcgcgaga agacttaact gatggttcac atgatgatgt totaaatgt 180  
 gaacaacttc agaaactcct ttacctgctg gagtcaacgg aggatactgt aattattgaa 240  
 agagctttga ttaactttgg taacaatgca gocttttcag ttaaccaage tattattcgt 300  
 gaattgggtg gtattccaat tgttgcaaac aaaatcaacc attccaacca gagtattaaa 360  
 25 gagaaagctt taaatgcact aaataacctg agtgtgaatg ttgaaatca aatcaagata 420  
 aaggtgcgaag ttttgaaact gcttttgaat ttgtctgaaa atccagccat gacagaagga 480  
 cttctccgtg cccaagtgga ttcacatcct ctttcccttt atgacagcca cgtagcaaaag 540  
 gagattcttc ttcgagtact tacgctattt cagaatataa agaactgcct caaantagaa 600  
 ggcatttagt ctgtgcagcc tactttcact gaaggttcat tgtttttcct gttacatgga 660  
 30 gaagaatgtg cccagaaaaa aagagcttta gttgatcacc atgatgcaga ggtgaaggaa 720  
 aaggttgtaa caataatcco caaaatc 747

&lt;210&gt; 48

&lt;211&gt; 294

35 &lt;212&gt; DNA





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ccagtgcgtga tcattggcat tctggtgttc ctaccggat ttaccacct ggcacgcgt 300  
tactatgcgt ccaaaggcta ccgtggttac tctatgatg acattccaga cttgatgac 360

<210> 51  
5 <211> 1065  
<212> DNA  
<213> Homo sapiens  
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10 <222> (2)...(943)

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Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly  
15 1 5 10 15  
tgg agt aca gat gag gct aat act tac ttc aag gaa tgg acc tgt tct 97  
Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
20 20 25 30  
tcg tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gac gaa tgt 145  
Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
35 40 45  
ect agt gca ttt gat ggc ctg tat ttt ctc cgc act gag aat ggt gtt 193  
Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
50 55 60  
25 atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241  
Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr  
65 70 75 80  
ctg gtg gcc agc gtg cat gag aat gac atg cgt ggg aag tgc acg gtg 289  
Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
30 85 90 95  
ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 337  
Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu  
100 105 110  
ggg gac ggc aac tgg gcc aac tac aac acc ttt gga tct gca gag gcg 385  
35 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala

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433	gpc agc agc agc gat gac tac aag aac cct ggc tac tac gac atc cag ggc	115	ala thr ser asp thr lys asn pro gly thr thr asp ile gln ala	120	125
481	aag gac cag ggc atc tgg cgc gtc aag tcc ccc atg cag cag	130		135	140
5		145	lys asp leu gly ile trp his val pro asn lys ser pro met gln his	150	155
10	trp arg asn ser ser leu leu arg thr asp thr gly phe leu	165		170	175
577	cag aac cag gga cat aat cag ttc ggc atc tac cag aaa tat cca tgg	180	gln thr leu gly his asn leu phe gly ile thr gln lys thr pro val	185	190
625	aaa tat gga gaa gga aag tgg act gac aac ggc ccg tgg atc cct	195	lys thr gly gln gly lys cys trp thr asp asn gly pro val ile pro	200	205
673	tgk gtc tat gat ttc ggc gac ggc cag aaa aca gca tct tat tac tca	210	val val thr asp phe gly asp ala gln lys thr ala ser thr thr ser	215	220
721	ccc tat ggc cag cgg gaa ttc act gcg gga ttc gtc cag ttc aag gta	225	pro thr gly gln arg gln phe thr ala gly phe val gln phe arg val	230	235
769	tct aat aac gag aga gca aac ggc tgg tgc gtc gga atg aag gtc	240		245	250
817	aac gga tgc aac act gaa cgc cgc tgc atc ggc gga gga gga tac ttc	255	phe asn asn gln arg ala ala asn ala leu cys ala gly met arg val	260	265
865	cca gag gcc agt ccc cag cag tgg gga gat ttc tct ggc ttc gat tgg	270		275	280
913	agt gga tat gga act cat gtc ggc tgc agc agc agc agc agc ata act	285	pro gln ala ser pro gln cys gly asp phe ser gly phe asp trp	290	295
960	gag gca gct gtc ctc cta ttc tat cgt tgaaggtttt gtaggggga	300	ser gly thr gly thr his val gly thr ser ser arg gln ile thr	305	310

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	Glu Ala Ala Val Leu Leu Phe Tyr Arg		
	305	310	
	accagacct ctctcccaa ccatgagatc ccaaggatgg agaacaactt acccagtagc		1020
	tagaatgtta atggcagaag agaaaacaat aatcatatt gactc		1065
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	tggagtttct tcagactcca gatttccttg tcaaccacga ggagtcacga gaggaacgc		120
	ggagcggaga caacagtacc tgacgcctct ttoagcccg gatgcacca gcaggg		176
	atg ggc gac aag atc tgg ctg ccc ttc ccc gtg ctg ctt ctg gcc gct		224
	Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala		
20	1	5	10
	ctg cct ccg gtg ctg ctg cct ggg gcg gcc gcc ttc aca cct tcc ctg		272
	Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu		
	20	25	30
	gat agc gac ttc acc ttt acc ctt ccc gcc gcc cag aag gag tgc ttc		320
25	Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe		
	35	40	45
	tac cag ccc atg ccc ctg aag gcc tcg ctg gag atc gag tac caa gtt		368
	Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val		
	50	55	60
30	tta gat gga gca gga tta gat att gat ttc cat ctt gcc tct cca gaa		416
	Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu		
	65	70	75
	ggc aaa acc tta gtt ttt gaa caa aga aaa tca gat gga gtt cac act		464
	Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr		
35	85	90	95

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512	Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe	110
560	Arg Acc Atc Tct Gaa Aag Gtg Atc Ttc Ttt Gaa Tta Atc Ctg Gat Mat	105
5	Ser Thr Ile Ser Glu Lys Val Ile Phe Glu Leu Ile Leu Asp Asn	125
608	Atg Gaa Gaa Caa Gaa Gaa Gaa Gat Tgg Aag Aaa Tat Atc Act	130
656	Ggc Acca Gat Ata Ttg Gat Atg Aaa Ctg Gaa Gac Atc Ctg Gaa Tcc Atc	140
10	Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Ser Ile	150
145	Aac Arg Atc Aag Tcc Aaa Cta Arg Aaa Agt Ggg Caa Ata Caa Atc Ctg	155
704	Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Glu Ile Leu	175
15	Ctt Aaa Gca Ttc Gaa Gct Cgt Gat Cga Aac Ata Caa Gaa Arg Aac Ttc	170
752	Ileu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Glu Glu Ser Asn Phe	185
800	Gat Aaa Gtc Aat Ttc Tgg Tct Atg Gtc Aat Tta Gtg Gtc Atg Gtg Gtg	190
848	Arg Val Asn Phe Ser Met Val Asn Leu Val Met Val Val	205
25	Arg Lys Ser Arg Thr	210
900	Arg Aaa Arg Aaa Act Taaaactcca aacttagagta cgttaacatcg aaaaatcg	220
30	aggatataaa atgcataataa ctgtacacagt caagagac	225
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&lt;222&gt; (56)...(1459)

&lt;400&gt; 53

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5	atg cgg ccc cag gag ctc ccc agg ctc gcg ttc cgg ttg ctg ctg ttg	103
	Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu	
	1 5 10 15	
	ctg ttg ctg ctg ctg cgg cgg cgg cgg tgc cct gcc cac agc gcc acg	151
10	Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr	
	20 25 30	
	cgc ttc gac ccc acc tgg gag tcc ctg gac gcc cgc cag ctg ccc gcg	199
	Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala	
	35 40 45	
	tgg ttt gac cag gcc aag ttc gcc atc ttc atc cac tgg gga gtg ttt	247
15	Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe	
	50 55 60	
	tcc gtg ccc agc ttc ggt agc gag tgg ttc tgg tgg tat tgg caa aag	295
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys	
	65 70 75 80	
20	gaa aag ata cgg aag tat gtg gaa ttt atg aaa gat aat tac cct cct	343
	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro	
	85 90 95	
	agt ttc aaa tat gaa gat ttt gga cca cta ttt aca gca aaa ttt ttt	391
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	
25	100 105 110	
	aat gcc aac cag tgg gca gat att ttt cag gcc tct ggt gcc aaa tac	439
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	
	115 120 125	
	att gtc tta act tcc aaa cat cat gaa ggc ttt acc ttg tgg ggg tca	487
30	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser	
	130 135 140	
	gaa tat tcg tgg aac tgg aat gcc ata gat gag ggg ccc aag agg gac	535
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp	
	145 150 155 160	
35	att gtc aag gaa ctt gag gta gcc att agg aac aga act gac ctg cgt	583

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1111	act ggg ccc aca cta gat ggc acc att cct gta gct ctt gag gag cga	345	Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg	350
1063	lys gln leu val glu thr val ser cys gly gly asn leu leu met asn	325	lys gln leu val glu thr val ser cys gly gly asn leu leu met asn	335
1015	agg agg gaa gct gga atc tct gac tat cct aca att gaa gaa tgg tgg	310	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val	320
25	cat aaa tgg gaa aac tgc acc atg aca ata gac aac ctt tgg ggc tat	295	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr	300
919	ggc ttc tat aac tgc agt gat cgt tat aac cca gga cat ctt tgg cca	280	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro	285
871	val val thr asn asp arg trp gly ala gly ser ile cys lys his gly	265	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly	270
823	gta gtc aac aat gat cgt tgg gga gct ggt agc atc tgt aag cat ggt	250	Gta Gtc Aac Aat Gat Cgt Tgg Gga Gct Ggt Agc Atc Tgt Aag Cat Ggt	255
775	acc ggc ttc tgg gcc tga tat aat gaa agc cca gtc cgg ggc aca	235	Ile Val Thr Asn Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr	240
727	acc tgg cca gag ctc tat gag tca gtc aac aac tat cag cct gag gct	215	Thr Leu Pro Glu Leu Tyr Glu Val Asn Asn Tyr Glu Pro Glu Val	220
679	gag gat gaa tcc agt tca ttc cat aag cgg cca ttc cca gtt tct aag	200	Glu Asp Glu Ser Ser Phe His Lys Arg Glu Phe Pro Val Ser Lys	205
631	ttt gga ctg tac tat tcc ctt ttt gaa tgg ttt cat ccg ctg ttc ctt	185	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu	190
		170		175
		165	Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg	

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ctg agg caa atg ggg tcc tgg cta aaa gtc aat gga gaa gct att tat 1159  
 Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr  
 355 360 365  
 gaa acc cat acc tgg cga tcc cag aat gac act gtc acc cca gat tgg 1207  
 5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val  
 370 375 380  
 tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ctt 1255  
 Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu  
 385 390 395 400  
 10 aaa tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att 1303  
 Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile  
 405 410 415  
 ctg ggg gca aca gag gtg aaa cta ctg ggc cat gga cag cca ctt aac 1351  
 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn  
 15 420 425 430  
 tgg att tct ttg gag caa aat ggc att atg gta gaa ctg cca cag cta 1399  
 Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu  
 435 440 445  
 acc att cat cag atg ccg tgt aaa tgg ggc tgg gct cta gcc ctg act 1447  
 20 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr  
 450 455 460  
 aat gtg atc taaagtgcag cagagtggct gatgctgcaa gttatgtcta aggc 1500  
 Asn Val Ile  
 465  
 25 taggaactat caggtgtcta taattgtaga acatggagaa agcaaatgta aaactggata 1560  
 agaaaattat ttggcagtt cagcccttto cctttttccc actaaatttt ttcttaaaatt 1620  
 acccatgtaa ccattttaac tctccagtgc accttgcgat taaagtctct tcacattg 1678  
  
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60	aggagagagagc ggtgcctccgc cgcggtgcgcg gtlgcctacgc ctcgcagaaa cctcctacagc	116	cagccagcctg agagagagctg agggagagctg ctgcctgcctg gtlcgcagac gcg atg	Met	1
164	gat aac gtc cag cag aaa ata aaa cat cgc ccc ttc tgc atc agt gtc	164	asp asn val gln pro lys ile lys his arg pro phe cys phe ser val	10	5
212	aaa ggc cac gtc agc atg ctg cgg ctg gat atc aac tca ctg gta	212	lys gly his val lys met leu arg leu asp ile asn ser leu val	10	10
260	aca aca gta ttc atg ctc atc gta tct gtc gtc gta cta cca gaa	260	thr thr val phe met leu ile val ser val leu ala leu pro gln	15	35
308	acc aca aca tgc aca gtc ggt gga ggg gtc gca ctt gca ctt gca aca gca	308	thr thr thr leu thr val gly gly val phe ala leu val thr ala	15	40
356	gta tgc tgc ctc ggc gac ggg gcc ctc atc tac cgg aag ctc ctg ttc	356	val cys cys leu ala asp gly ala leu ile tyr arg lys leu leu phe	20	50
404	aat ccc aag ggt cct tac cag cag aag cct gtc cat gaa aaa gaa	404	asn pro ser gly pro tyr gln lys pro val his gln lys lys gln	20	55
450	gct ttc taatttata ttaactttcta gtttgact aagatataa	450	val leu	25	60
467	catattctcg tattctt	467		30	65
30	<210> 55			35	70
	<211> 875			40	75
	<212> DNA			45	80
	<213> Homo sapiens			50	85
	<220>			55	90
35	<221> CDS			60	95



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&lt;222&gt; (272)...(841)

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 ggggtcgtcg gattgaggtc ccggttccta acgaatctct gctggattgg ccgtaacct 180  
 gtcccgcagc gggtcacag ggtctgaag ccacgcata ggcaaaggt aagttctgag 240  
 ccaccgggtg cctccttccc aggactgcaa g atg gag gaa gcc ggg aac cta 292  
 Met Glu Glu Gly Gly Asn Leu  
 10 1 5  
 gga gcc ctg att aag atg gtc cat cta ctg gtc ttg tca ggt gcc tgg 340  
 Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp  
 10 15 20  
 ggc atg caa atg tgg gtg acc ttc gtc tca gcc ttc ctg ctt ttc cga 388  
 15 Gly Met Gln Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg  
 25 30 35  
 agc ctt ccc cga cat acc ttc gga cta gtg cag agc aaa ctc ttc ccc 436  
 Ser Leu Pro Arg His Thr Phe Gly Leu Val Gln Ser Lys Leu Phe Pro  
 40 45 50 55  
 20 ttc tac ttc cac atc tcc atg gcc tgt gcc ttc atc aac ctc tgc atc 484  
 Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile  
 60 65 70  
 ttg gct tca cag cat gct tgg gct cag ctc aca ttc tgg gag gcc agc 532  
 Leu Ala Ser Gln His Ala Trp Ala Gln Leu Thr Phe Trp Glu Ala Ser  
 25 75 80 85  
 cag ctt tac ctg ctg ttc ctg agc ctt acg ctg gcc act gtc aac gcc 580  
 Gln Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala  
 90 95 100  
 cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc 628  
 30 Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Gln Thr  
 105 110 115  
 gtg gag aag gag cga gcc ctg ggt ggg gag gta cca gcc agc cac cag 676  
 Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Gln  
 120 125 130 135  
 35 ggt ccc gat ccc tac cgc cag ctg cga gag aag gac ccc aag tac agt 724

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35	Ala Pro Arg Thr Phe Thr Leu Leu Asp Pro Lys Ala Ser Leu Leu Thr	45	50	55
	gac cct cgg acc ctt acc ctt ctg gac ccc aag gca tct ctg tta acc	25	30	35
30	Gln Ser His Pro Asp Leu Gly Thr Glu Gly Cys Trp Asp Gln Leu Ser	40	45	50
	cag aag cat cca gac act gag ggc tgc tgg gac cag ctc tct	20	25	30
25	Thr Leu Ala Gly Asn Leu Gly Leu Thr Phe Leu Arg Gly Ser Gln Thr	10	15	20
	acc ctg gct gga aac ctg ggc ctg gac ttc ctc cga ggt tcc cag acc	5	1	5
20	Mat Val Asp Ser Leu Ala Val	5	1	5
	ccagatgccaaa agccaaagttcc ccacccgaccc atg gtc gac agc ctc ctg gca gtc	173	120	60
15	atgttaagagc caccctccctcc ccagagactcca gggatggcttc tccagatgtc acccaatgtcag	173	120	60
	atcatgtggagc caaacactcca gatgctacaaa aaggctgttcc agatgtccaaa gttctctctgc	173	120	60
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	<400> 56			
10	Leu Glu Ile Arg Ser Leu	185		
	ctg gaa tta aag agc ctc tagcatgggc cctgcattgct aataaattgct tcttcag	875		
5	Asn Leu Gly Cys Val Leu Ser Asn Gly Leu Cys Leu Ala Gly Leu Ala	170	175	180
	aat ctg ggc tgc gtc ctg aag cat ggg ctc tgt ctc gct ggc ctc ggc	820		
5	Ala Leu Arg Gln Asn Phe Thr Phe Arg Tyr His Gly Leu Ser Ser Leu Cys	155	160	165
	gct ctc cgc cag aat ttc ctc cgc tac cat ggg ctg tcc tct ctt tgc	772		
5	Gly Pro Asp Pro Tyr Arg Gln Leu Arg Gln Lys Asp Pro Lys Tyr Ser	140	145	150

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	aag gcc ttc ctc aat ggc gcc ctg gat ggg gtc atc ctt gga gac tac	365
	Lys Ala Phe Leu Asn Gly Ala Leu Asp Gly Val Ile Leu Gly Asp Tyr	
	60 65 70	
	ctg agc cgg act cct gag ccc cgg cca tcc ctc agc cac ttg ctg agc	413
5	Leu Ser Arg Thr Pro Glu Pro Arg Pro Ser Leu Ser His Leu Leu Ser	
	75 80 85	
	cag tac tat ggg gct ggg gtg gcc aga gac coa ggg ttc cgc agc aac	461
	Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn	
	90 95 100	
10	ttc cga cgg cag aac ggt gct gct ctg act tca gcc tcc atc ctg gcc	509
	Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala	
	105 110 115 120	
	cag cag gtg tgg gga acc ctt gtc ctt cta cag agg ctg gag coa gta	557
	Gln Gln Val Trp Gly Thr Leu Val Leu Gln Arg Leu Glu Pro Val	
15	125 130 135	
	cac ctc cag ctt cag tgc atg agc caa gaa cag ctg gcc cag gtg gct	605
	His Leu Gln Leu Gln Cys Met Ser Gln Glu Gln Leu Ala Gln Val Ala	
	140 145 150	
	gcc aat gct acc aag gaa ttc act gag gcc ttc ctg gga tgc cgc gcc	653
20	Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala	
	155 160 165	
	atc cac ccc cgc tgc cgc tgg gga gcg gcg cct tat cgg ggc cgc cgc	701
	Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro	
	170 175 180	
25	aag ctg ctg cag ctg ccg ctg gga ttc ttg tac gtg cat cac acc tac	749
	Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr	
	185 190 195 200	
	gtg cct gca cca ccc tgc acg gac ttc acg cgc tgc gca gcc aac atg	797
	Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met	
30	205 210 215	
	cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc	845
	Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile	
	220 225 230	
	ggc tac agt ttc gtg gtg ggc tgc gac gcc tac gtg tac gag gga cgc	893
35	Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg	

235 240 245

5	tlc ggc gtc gcc ata gtc ggc aac tac aac gcc ggc ggc ctc gcc aac gag	989
	phe gly val ala ile val gly asn tyr thr ala ala leu pro thr glu	
265		
270		
275		
280		

1085	gac ggc ctc ctc cgc cga gac tac ggc ctc ctc ggc cgc cgc cgc cgc	Ala Gly Leu Leu Arg Pro Asp Tyr Ala Leu Leu Gly His Arg Gln Leu	300
			305
			310

181	tyg ceg cae tlc acc gcg act gtt mag cga aga cct gcc agy agt gtc	330	trp pro his phe thr ala thr val lys pro arg pro ala arg ser val	340
				335

1256

30 <220>  
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<400> 57

09

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	gcgcggggcg cagc atg ggt ggc ccc cgg ggc ggc tgg gtg gcg gcg	170
	Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala	
	1 5 10	
5	ggc ctg ctg ctc ggc ggc ggc gcc tgc tac tgc att tac agg ctg acc	218
	Gly Leu Leu Leu Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr	
	15 20 25	
	cgg ggt cgg cgg cgg ggc gac cgc gag ctc ggg ata cgc tct tcg aag	266
	Arg Gly Arg Arg Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys	
10	30 35 40	
	tcc gca gaa gac tta act gat ggt tca tat gat gat gtt cta aat gct	314
	Ser Ala Glu Asp Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala	
	45 50 55 60	
	gaa caa ctt cag aaa ctc ctt tac ctg ctg gag tca acg gag gat cct	362
15	Glu Gln Leu Gln Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro	
	65 70 75	
	gta att att gaa aga gct ttg att act ttg ggt aac aat gca gcc ttt	410
	Val Ile Ile Glu Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe	
	80 85 90	
20	tca gtt aac caa gct att att cgt gaa ttg ggt ggt att cca att gtt	458
	Ser Val Asn Gln Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val	
	95 100 105	
	gca aac aaa atc aac cat tcc aac cag agt att aaa gag aaa gct tta	506
	Ala Asn Lys Ile Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu	
25	110 115 120	
	aat gca cta aat aac ctg agt gtg aat gtt gaa aat caa atc aag ata	554
	Asn Ala Leu Asn Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile	
	125 130 135 140	
	aag gtg caa gtt ttg aaa ctg ctt ttg aat ttg tct gaa aat cca gcc	602
30	Lys Val Gln Val Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala	
	145 150 155	
	atg aca gaa gga ctt ctc cgt gcc caa gtg gat tca tca ttc ctt tcc	650
	Met Thr Glu Gly Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser	
	160 165 170	
35	ctt tat gac agc cac gta gca aag gag att ctt ctt cga gta ctt acg	698

15	<p>&lt;210&gt; 58</p> <p>&lt;211&gt; 589</p> <p>&lt;212&gt; DNA</p> <p>&lt;213&gt; Homo sapiens</p>	10	<p>&lt;220&gt;</p> <p>&lt;221&gt; CDS</p> <p>&lt;222&gt; (48)...(344)</p>	25	<p>&lt;400&gt; 58</p>	35	<p>Leu Tyr Asp Ser His Val Ala Lys Glu Ile Leu Leu Arg Val Thr</p> <p>175</p> <p>180</p> <p>185</p>	40	<p>cta ttc cag aat ata aag aac tgc aca ata gaa ggc cat tta gct</p> <p>Leu phe gln asn ile lys asn cys leu lys ile glu gly his leu ala</p> <p>190</p> <p>195</p> <p>200</p>	45	<p>gfg cgc act ttc act gaa ggt tca tcy ttc ttc cty tta cat gga</p> <p>Val gln pro thr phe thr glu gly ser leu phe leu his gly</p> <p>205</p> <p>210</p> <p>215</p> <p>220</p>	50	<p>gaa gaa tgc gcc cag aaa ata aga gct tta gtt gat cac gat gaa</p> <p>glu glu cys ala glu lys ile arg ala leu val asp his asp ala</p> <p>225</p> <p>230</p> <p>235</p>	55	<p>gag gty aag gaa aag gtt gta aca ata ccc aaa atc tga</p> <p>glu val lys glu lys val val thr ile ile pro lys ile</p> <p>245</p>	60	<p>Met Ala Ser</p> <p>1</p>	65	<p>ctc tcy tgc tgc ggg ccg aag ctg gcc gcc tcy gcc atc ctc agc</p> <p>Leu leu cys cys gly pro lys leu ala ala cys gly ile val leu ser</p> <p>5</p> <p>10</p> <p>15</p>	70	<p>gcc tcy gaa gty atc atc tcy ata atc gga atc ttc ttc atc gtc</p> <p>Ala trp gly val ile Met leu ile Met leu gly ile phe phe asn val</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p>	75	<p>cat tcc gcc tcy tcy atc gty gac gtc ccc ttc aag gag aaa gat ttc</p> <p>His ser ala val leu ile glu asp val pro phe thr glu lys asp phe</p> <p>200</p>
----	---	----	---	----	-----------------------	----	---	----	--	----	---	----	--	----	--	----	-----------------------------	----	--	----	---	----	--

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	40	45	50	
	gag aat ggc ccc cag aac ata tac aac ctt tac gag caa gtc agc tac			248
	Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln Val Ser Tyr			
	55	60	65	
5	aac tgt ttc atc gct gca ggc ctt tac ctc ctc gga ggc ttc tct			296
	Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser			
	70	75	80	
	ttc tgc caa gtt cgg ctc aat aag cgc aag gaa tac atg gtg cgc			341
	Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met Val Arg			
10	85	90	95	
	tagggcccc ggcgcggttc ccgcgtccag cccctcctct atttaaagac tccctgcaac			400
	gtgtcaccca ggtcgcgctc cacccttgcc ggcgccctct gtgggactgg gttcccggg			460
	cgagagactg aatcccttct cccatctctg gcacccggcc cccgtggaga gggctgaggg			520
	tgggggcgctg ttcctctctt ccaccccttg ctgtgtcccg tatctcata aagagaatct			580
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	Met Val Gly Pro Ala Pro Arg Arg Arg			
	1	5		
	ctg cgg cgg ctg gca gcg ctg gcc ctg gtc ctg gcg ctg gcc cgg ggg			99
30	Leu Arg Pro Leu Ala Ala Leu Ala Leu Val Leu Ala Leu Ala Pro Gly			
	10	15	20	25
	ctg ccc aca gcc cgg gcc ggg cag aca ccg cgc cct gcc gag cgg ggg			147
	Leu Pro Thr Ala Arg Ala Gly Gln Thr Pro Arg Pro Ala Glu Arg Gly			
	30	35	40	
35	ccc cca gtg cgg att ttc acc gag gag gag ctg gcc cgc tat ggc ggg			195

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	<211> 1425	
	<212> DNA	
	<213> Homo sapiens	
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	10	
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&lt;222&gt; (127)...(489)

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5	gccaacctg ggcgagctct ggggtgcgg gcggcctggc gcggcgctcc gctgtgtcag	120
	cgtgtt atg atg ccg tcc cgt acc aac ctg gct act gga atc ccc agt	168
	Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser	
	1 5 10	
	agt aaa gtg aaa tat tca agg ctc tcc agc aca gac gat ggc tac att	216
10	Ser Lys Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile	
	15 20 25 30	
	gac ctt cag ttt aag aaa acc cct cct aag atc cct tat aag gcc atc	264
	Asp Leu Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile	
	35 40 45	
15	gca ctt gcc act gtg ctg ttt ttg att ggc gcc ttt ctc att att ata	312
	Ala Leu Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile	
	50 55 60	
	ggc tcc etc ctg ctg tca ggc tac atc agc aaa ggg ggg gca gac cgg	360
	Gly Ser Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg	
20	65 70 75	
	gcc gtt cca gtg ctg atc att ggc att ctg gtg ttc cta ccc gga ttt	408
	Ala Val Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe	
	80 85 90	
	tac cac ctg cgc atc get tac tat gca tcc aaa ggc tac cgt ggt tac	456
25	Tyr His Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr	
	95 100 105 110	
	tcc tat gat gac att cca gac ttt gat gac tagcaccac ccca	500
	Ser Tyr Asp Asp Ile Pro Asp Phe Asp Asp	
	115 120	
30	tagctgagga ggagtcacag tggaactgtc ccagctttaa gatattagc agaaactata	560
	gctgaggact aaggaattct gcagcttgca gatgtttaag aaaataatgg ccagattttt	620
	tgggtccttc ccaaatgtgt taagtgaacc tacagttagc taattagagc aagctotatt	680
	tttcatccct gggccctgac aagtttttcc acaggaatat gtatcatgga agaataagag	740
	ttattctgta atggaaaagt gttgcctgcc accaccctct gttagagctga gcatttcttt	800
35	taaatagtct tcattgocaa tttgttctgt tagcaaatgg aacaatgtgg tatggctaat	860

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920	tctctatcat taagtagtattt attcttaaaaa tatctagtaga tattatccctg taccatctac
980	cttaccctcaa tgttccagagt gaagaccctta gtaaatctcaa agatcagatga gttcattcgt
1040	aatatttttt tcaattgctt tcttacttagc agcaaaccaag aattttttta tccctgcagaa
1100	caagtgttcaa aaatgttaaat acttccctctg ttcaaacagtc cttggaccat tctgattccag
1160	ttcaaccagta ggttgygaacg catataattt gcatcatttt gtcccttctga atacaagaatg
1220	ttctgcagat tatctccctta accgcccgagc ttttggcgtg tttctaatga aaccatagat
1280	ggttatattc tagaatttat agccgtaattg ctaggaccctt gtagtatagtc atccattctgc
1340	tcatgatctcc aagagatccg ctggatgctc agaggagctag atccacctag ttgatctcaa
1400	tttttttagct tgcnaaaagt gacttatatt ccaaggaatat taatatgttg aaattccaaat
1425	ctagaatatc aatatgagta actc

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 <212> PRT  
 <213> Homo sapiens

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 Pro Leu Ser Ala Ser Thr Asp Tyr Glu Ser Thr Gly Met Glu  
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 Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Glu Leu Pro  
 35  
 40  
 45  
 Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser  
 55  
 60  
 Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr Pro Asn  
 65  
 70  
 75  
 Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Lys Glu Phe Ile Thr  
 80  
 85  
 90  
 95  
 Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe  
 100  
 105  
 110  
 Ile Glu Phe Asp Asn Phe Ile Glu Arg Thr Lys Glu Arg Tyr Asn Asn  
 115  
 120  
 125  
 Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Glu Thr Glu  
 130  
 135  
 140

35

30

25

20

15

10

5

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Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser  
 145 150 155 160  
 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly  
 165 170 175  
 5 Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly  
 180 185 190  
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile  
 195 200 205  
 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp  
 10 210 215 220  
 Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys Leu Tyr  
 225 230 235 240  
 Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val Lys Ser  
 245 250 255  
 15 Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu  
 260 265 270  
 Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly Ala Phe  
 275 280 285  
 Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala Pro Asp  
 20 290 295 300  
 Tyr Asp Val  
 305  
  
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 25 <211> 183  
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 <213> Homo sapiens  
  
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 Trp Ala Ile Glu Leu Ser Gly Pro Gly Gly Gly Ser Arg Gly Arg Ser  
 20 25 30  
 Asp Arg Gly Ser Gly Gln Gly Asp Ser Leu Tyr Pro Val Gly Tyr Leu  
 35 40 45

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35	65	70	75	80
	50	55	60	
	35	40	45	
	20	25	30	
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	1	5	10	15
	1	5	10	15
	1	5	10	15
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	<211> 327			
	<212> PRT			
20	<213> Homo sapiens			
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	165	170	175	
	145	150	155	160
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	115	120	125	130
	100	105	110	115
	85	90	95	100
10	70	75	80	85
	55	60	65	70
	40	45	50	55
	25	30	35	40
5	10	15	20	25
	5	10	15	20
	1	5	10	15
	1	5	10	15

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Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr Ser Gly Asp Leu  
85 90 95

Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu Gln Leu Glu Asn  
100 105 110

5 Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr Thr Gln Tyr Arg  
115 120 125

Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe  
130 135 140

Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Glu  
10 145 150 155 160

Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr  
165 170 175

Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp  
180 185 190

15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn  
195 200 205

Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr Lys Leu Lys Ile  
210 215 220

Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp Cys Arg Ala Leu  
20 225 230 235 240

Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu Val Val Leu Ser  
245 250 255

Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val Ala Glu Val Ile  
260 265 270

25 Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr Thr Gln Lys Lys  
275 280 285

Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln Ile Glu Gln Leu  
290 295 300

Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val Pro Arg His Arg  
30 305 310 315 320

Lys Asn Glu Ser Leu Gly Gln  
325

&lt;210&gt; 64

35 &lt;211&gt; 223

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<212> PRT  
<213> Homo sapiens

<400> 64

Met Lys Phe Val Pro Cys Leu Leu Val Thr Leu Ser Cys Leu Gly

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Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Gln

20 25 30

Phe His Phe Gln Thr Gly Arg Asp Ser Cys Thr Met Arg Pro Ser

35 40 45

Ser Leu Gly Gln Gly Ala Gly Gln Val Thr Leu Arg Val Asp Cys Arg

50 55 60

Asn Thr Asp Gln Thr Tyr Trp Cys Gln Tyr Arg Gly Gln Pro Ser Met

65 70 75 80

Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala Leu

85 90 95

Gln Gln Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val Leu

100 105 110

Arg Pro Ser Val Cys Arg Gln Ala Gly Pro Gln Ala His Met Gln Gln

115 120 125

Val Thr Ser Ser Leu Lys Gly Ser Pro Gln Pro Asn Gln Gln Pro Gln

130 135 140

Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr Gln

145 150 155 160

Ala Thr Gln Leu Gly Lys Asp Ser Met Gln Gln Leu Gly Lys Ala Lys

165 170 175

Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg Pro

180 185 190

Gly Gly Asn Gln Gln Ala Lys Lys Lys Ala Trp Gln His Cys Trp Lys

195 200 205

Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Arg Gly

210 215 220

35 <210> 65

<211> 48

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

5 Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg  
 1 5 10 15  
 Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys  
 20 25 30  
 10 Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
 35 40 45

&lt;210&gt; 66

&lt;211&gt; 371

&lt;212&gt; PRT

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 66

Met Ala Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val  
 1 5 10 15  
 20 Thr Gly Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met  
 20 25 30  
 Ala Glu Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe  
 35 40 45  
 25 Leu Gln Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala  
 50 55 60  
 Phe Tyr Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val  
 65 70 75 80  
 Asp Pro Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu  
 85 90 95  
 30 Cys Asp Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr  
 100 105 110  
 Ser Ala Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr  
 115 120 125  
 35 Gly Leu Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Ser Gln  
 130 135 140

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35	<210> 67 <211> 90 <212> PRT <213> Homo sapiens
30	asp ala ser 370
25	355 340 345 350 335 330 315 310 295 300 285 280 275 260 265 250 255 245 230 235 225 220 215 210 200 205 195 180 185 190 175 170 165 160 155 150 145
20	trp leu gly ile leu ala thr ile ala gly leu val val val gly leu ala thr thr arg met val leu asp ser leu arg thr val ile trp ala leu ser leu ala leu gly trp glu ala phe ala leu glu ile leu gly phe leu ile leu leu ile gly thr ala leu tyr asn gly leu ile ala phe phe asn phe ala gly ile ser val thr lys glu leu ser gly glu pro leu ile ala val ala leu leu gly asn ile ser ser asn pro arg gly thr leu glu asp ala leu asp ala phe cys glu val leu leu leu val pro met tyr tyr ile pro ala gly ser phe ser gly leu arg ala val gly thr glu gly leu phe gly phe val ile leu ser gin met val leu glu glu lys phe val tyr lys his asn val his pro ile thr gly asp leu leu ile ile met ala glu ile ile ala ile
15	
10	
5	



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<400> 67  
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 5 Leu Asn Ser Ile Tyr Gln Cys Pro Glu His Ser Gln Leu Thr Thr Leu  
 20 25 30  
 Gly Val Asp Gly Lys Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr  
 35 40 45  
 Phe Ile Ala Gly Ala Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp  
 10 50 55 60  
 Pro Val Asp Asn Ile Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met  
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 Gln Leu His Leu Arg Ala Thr Ile Arg Met  
 85 90  
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 25 20 25 30  
 Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu  
 35 40 45  
 Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val  
 50 55 60  
 30 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe  
 65 70 75 80  
 Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile  
 85 90 95  
 Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg  
 35 100 105 110

[illegible]

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385                      390                      395                      400  
 Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln  
                                  405                      410                      415  
 Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu  
 5                                   420                      425                      430  
 Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser  
                                  435                      440                      445  
 Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe  
                                  450                      455                      460  
 10 Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser  
                                  465                      470                      475                      480  
 Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro  
                                  485                      490                      495  
 Lys Gly Thr  
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 <210> 69  
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 20 <213> Homo sapiens  
  
 <400> 69  
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 25 Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr Arg Glu Lys Leu Thr Pro  
                                  20                      25                      30  
 Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Ala Gln Trp Gln Lys  
                                  35                      40                      45  
 Val Leu Pro Arg Arg Arg Thr Arg Asn Ile Val Thr Gly Leu Gly Ile  
 30                      50                      55                      60  
 Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr Thr Phe Tyr Ser Ile Ser  
                                  65                      70                      75                      80  
 Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp Glu Ala Lys Ala Ala Arg  
                                  85                      90                      95  
 35 Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser

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		15
	Ala Gln Lys Gly Lys Ser Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile	20
		25
		30
		35
		40
		45
15	Ser Leu Phe Leu Ile Ile Ser Met Cys Leu Leu Phe Leu Trp Lys Lys	50
		55
		60
	Tyr Gln Pro Tyr Lys Val Ile Lys Gln Lys Leu Gln Gly Arg Pro Gln	65
		70
		75
		80
	Thr Gln Tyr Arg Lys Ala Gln Thr Phe Ser Gly His Gln Asp Ala Leu	85
		90
		95
20	Asp Asp Phe Gly Ile Tyr Gln Phe Val Ala Phe Pro Asp Val Ser Gly	100
		105
		110
	Val Ser Arg Ile Pro Ser Arg Ser Val Pro Ala Ser Asp Cys Val Ser	115
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	Gly Gln Asp Leu His Ser Thr Val Tyr Gln Val Ile Gln His Ile Pro	130
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		140
		145
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	<213> Homo sapiens	
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	tggaggaaac ttgctcaact toctgataga tgtacaotga aaactggaca ttataacatt	180
	aattttatta gctctctggg agtgagctac atgatgtgtg gcactgaaa ttacccaant	240
5	gttctcgctt totctttcct ggatgagott cagaaggagt tcattactac ttataacatg	300
	atgaagacaa atactgctgt cagaccatac tgtttcattg aatttgataa cttcattcag	360
	aggaccacagc agcgatataa taatcccagg tctctttoa caaagataaa tctttctgac	420
	atgcagacgg aaatcaagct gaggcctcct tatcaaatat ccatgtgca actggggcca	480
	gccaatggag tcacatcagc attttctgtt gactgtaaag gtgctggtaa gatttcttct	540
10	gctcacacgc gactggaacc agcaactctg tcagggattg taggatttat ccttagtctt	600
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	gatggtgatg attttaatta catcattgca ttttctctg gaacagcagc ctgcctttac	720
	cagtgttatt taactgtcta ctacaccggc tggcggaatg tcaaatcttt tttagctttt	780
	ggtttaatct gtctatgcaa catgtatctc tatgaaactg gcaacctctg gcagcttttc	840
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	tcgctctacc cagtcgggta cttggacaag caagtgcctg ataccagctg gcaagagaca	180
	gacccgatcc tgggtggagaa gcgctgctgg gacatgcctt tgggtccctt caaacagatt	240
	cccatgaatc tcttcattcat gtacatggca ggcataacta tctccattct cctactatg	300
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	ctgctttttg	549
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720	800
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540	650
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420	550
360	500
300	450
240	400
180	350
120	300
60	250

360	agagc
300	agag
240	agc
180	cgc
120	gag
60	gac

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	ggacccagg cccatatgca gcaggtgact tccagcctca agggcagccc agagcccaac	420
	cagcagcctg aggtggggac gccatctctg agggccaagg ccacagtga actcacagaa	480
	gcaacacagc tgggaaagga ctcgatggaa gagctgggaa aagccaaacc caccaccoga	540
	cccacagcca aacctaccca gctgggaccc aggcocggag ggaatgagga agcaagaag	600
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	gagcagagct tccagcatcc ctctctccag gcagtgggca tgttctggg agaattctcc	180
	tgcttggtcg cttctacct cctccgatgc agagctgca ggaataaga ctccagcgtc	240
	gaccccccag agcccttcaa cctcttctt ttctgcccc cagcgtctg tgacatgaca	300
	gggaccagcc tcattgatgt ggctctgaac atgaccagt cctccagct ccagatgctg	360
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	gtgctgagcc agtggctggg catcctagcc accatcgcg ggtggtggt cgtgggctg	480
	gctgacctcc tgagcaagca cgacagtcag cacaagctca gcgaagtgat cacaggggac	540
	ctgttgata tcattgcccc gatcatggt gccatcoaga tggctgtaga ggagaagttc	600
	gtctacaaac acaattgcca cccactgcgg gcagttggca ctgagggct ctttgcttt	660
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[illegible]



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	gccctgtacc gctacttcgt ggagctctgg atctacttgg ggcctggcctg gctgtccctt	720
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15	atggcgagt tccccctctc ctccagagtc acctcaacca gcactgagtc tgagctctct	1440
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	gcggaacttg cccagtggca gaaggtccta ccacggcggc gaaccgggaa catcgtgacc	180
	ggcctagga cctggggccct ggtgttggtt atttatggtt acaactttta ctgatttcc	240
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30	50	55	60	Ileu Pro Asp Arg Cys Thr Ileu Lys Thr Gly His Tyr Asn Ile Asn Phe cct cct gat aga tgc aca cct gga aat gga cat tat aac att aat tct	251
	35	40	45	Gln Glu Cys Arg Lys Tyr Phe Lys Met Ileu Ser Arg Lys Ileu Ala Gln caa gag tgc aga aag tat tct aaa atg cct tgc agg aaa ctt gtc caa	203
	15	20	25	Gly Ileu Pro Ileu Ser Ala Ser Tyr Asp Tyr Glu Gln Ser Thr Gly Met gga cct cca cct tct gct tct act gat tat gaa caa aga aca gga atg	155
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	acgtatctaca tcaactccgt aggaactcgag aagcttcgaac agaaagagaa aatcaatctca ccttatgacaa gtaatacctgg aataacacaa tttttgacta taatccaatgtg tcttctctc	acgtatctaca tcaactccgt aggaactcgag aagcttcgaac agaaagagaa aatcaatctca			420
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	att act act tat aac atg atg aag aca aat act gct gtc aga cca tac	395
5	Ile Thr Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr	
	95 100 105 110	
	tgt ttc att gaa ttt gat aac ttc att cag agg acc aag cag cga tat	443
	Cys Phe Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr	
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10	aat aat ccc agg tct ctt tca aca aag ata aat ctt tct gac atg cag	491
	Asn Asn Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln	
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	acg gaa atc aag ctg agg cct cct tat caa att tcc atg tgc gaa ctg	539
	Thr Glu Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu	
15	145 150 155	
	ggg tca gcc aat gga gtc aca tca gca ttt tct gtt gac tgt aaa ggt	587
	Gly Ser Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly	
	160 165 170	
	gct ggt aag att tct tct gct cac cag cga ctg gaa cca gca act ctg	635
20	Ala Gly Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu	
	175 180 185 190	
	tca ggg att gta gga ttt atc ctt agt ctt tta tgt gga gct ctg aat	683
	Ser Gly Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn	
	195 200 205	
25	tta att cga ggc ttt cat gct ata gaa agt ctc ctg cag agt gat ggt	731
	Leu Ile Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly	
	210 215 220	
	gat gat ttt aat tac atc att gca ttt ttc ctt gga aca gca gcc tgc	779
	Asp Asp Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys	
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	ctt tac cag tgt tat tta ctt gtc tac tac acc ggc tgg cgg aat gtc	827
	Leu Tyr Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val	
	240 245 250	
	aaa tct ttt ttg act ttt ggc tta atc tgt cta tgc aac atg tat ctc	875
35	Lys Ser Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu	

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[illegible]

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5	tct tgt ttc ttt cga gag gaa aag gaa caa agg gga aca ttt aat ttc	601		
	Ser Cys Phe Phe Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe			
	145 150 155			
	aaa gtc cct gaa ctt cat ggg aaa aac aag cca ttg atc tct tac gta	649		
	Lys Val Pro Glu Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val			
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	ggg gat tct act gtc ttg aca tgt aaa tgt caa aat tgt ttt cct tta	697		
	Gly Asp Ser Thr Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu			
	175 180 185			
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15	Asn Trp Thr Trp Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly			
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	gtt caa atg aat aaa tat gtg atc aat gga aca tat gct aac gaa aca	793		
	Val Gln Met Asn Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr			
	205 210 215 220			
20	aag ctg aag ata aca caa ctt ttg gag gaa gat ggg gaa tct tac tgg	841		
	Lys Leu Lys Ile Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp			
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	Cys Arg Ala Leu Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu			
25	240 245 250			
	gtg gtg ctg agc tat ttg gtg ccc ctc aaa cca ttt ctt gta ata gtg	937		
	Val Val Leu Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val			
	255 260 265			
	gct gag gtg att ctt tta gtg gcc acc att ctg ctt tgt gaa aag tac	985		
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	270 275 280			
	aca caa aag aaa aag aag cac tca gat gag ggg aaa gaa ttt gag cag	1033		
	Thr Gln Lys Lys Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln			
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35	att gaa cag ctg aaa tca gat gat agc aat ggt ata gaa aat aat gtc	1081		

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35	gaa ttc cat ttc cag act gga agg aga gat tcc tgc acc atg cgt ccc	gln phe his phe gln thr gly arg asp ser cys thr met arg pro	202	
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106	c atg aag ttc gtc ccc tgc ctc ctg ctg gtc acc tgc tcc tgc ctg	met lys phe val pro cys leu leu val thr leu ser cys leu	106	
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	1670			
	1610			
	1550			
	1490			
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	1370			
	1310			
	1250			
	1190			
5	320	325		
	tgctcagagat catctggaaaga tatcaagagat tccgtattca gctttattta tccctccgtg	tgctcagagat catctggaaaga gattctaaag gattgcnaaagc ttaattgcacaaa tgcctcaagcag	1190	
	1130			
	ccc aag cat aga aaa aat gag tct ctg ggc cag tgaatacaaaa acatca	pro arg his arg lys asn gln ser leu gly gln	1130	
	305	310	315	
	ile gln gln leu lys ser asp asp ser asn gly ile gln asn asn val			



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	Ser Ser Leu Gly Gln Gly Ala Gly Glu Val Trp Leu Arg Val Asp Cys			
	50 55 60			
5	cgc aac aca gac cag acc tac tgg tgt gag tac agg ggg cag ccc agc	298		
	Arg Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser			
	65 70 75			
	atg tgc cag gct ttc gct gct gac ccc aaa tct tac tgg aat caa gcc	346		
	Met Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala			
10	80 85 90 95			
	ctg cag gag ctg agg cgc ctt cac cat gcg tgc cag ggg gcc ccg gtg	394		
	Leu Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val			
	100 105 110			
	ctt agg cca tcc gtg tgc agg gag gct gga ccc cag gcc cat atg cag	442		
15	Leu Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln			
	115 120 125			
	cag gtg act tcc agc ctc aag ggc agc cca gag ccc aac cag cag cct	490		
	Gln Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro			
	130 135 140			
20	gag gct ggg acg cca tct ctg agg ccc aag gcc aca gtg aaa ctc aca	538		
	Glu Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr			
	145 150 155			
	gaa gca aca cag ctg gga aag gac tcg atg gaa gag ctg gga aaa gcc	586		
	Glu Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala			
25	160 165 170 175			
	aaa ccc acc acc cga ccc aca gcc aaa cct acc cag cct gga ccc agg	634		
	Lys Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg			
	180 185 190			
	ccc gga ggg aat gag gaa gca aag aag aag gcc tgg gaa cat tgt tgg	682		
30	Pro Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp			
	195 200 205			
	aaa ccc ttc cag gcc ctg tgc gcc ttt ctc atc agc ttc ttc cga ggg	730		
	Lys Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly			
	210 215 220			
35	tgacaggtga aagacccta cagatctgac ctctccctga cagacaacca tctcttttta	790		

5 tatcatgccc cttccatccc aacgtctccc caactggaaga agagaagtttc tcaatcagaagtg 850  
 ccaagggccc aattcttgat ctggcagcttc tctgaaattc ggaagaagaa cctctcttc 910  
 tggagttctg agagttctagc aatctgataag ggaacagcttg ctgagtggtc caaagtgtaac 970  
 aagctatacc aactacttat tatctgtaga agttctgtctc tgttgatctg agcctctcat 1030  
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 Met Arg Leu Leu 1  
 ctg ctt cta ctg gct gct tct gct atg gtc cgt agc gag gct tctg 102  
 Leu Leu Leu Val Ala Met Val Arg Ser Glu Ala Ser  
 5 10 15 20  
 gcc aat ctg ggc ggc gtc gcc agc aag aca aag atg cag taa gcc 150  
 Ala Asn Leu Gly Val Pro Ser Lys Arg Leu Lys Met Glu Tyr Ala  
 25 30 35  
 aag ggg ccg ctg ctc aag ttc aag att tgt gtt tcc tgg 190  
 Thr Gly Pro Leu Leu Lys Phe Glu Ile Cys Val Ser  
 40 45

gttataagggc ggtgtctgag ggtatcaatgc ggttatctag caagcgttac caagaaatcc 250  
 gcatctgaag agagaattcac ctcctccaac caatataatag acaataataga tcttctcctgt 310  
 caatctccaa aactagttcaa ataggtctcaa taaattgtctgg caaggtatcct tctgctctctc 370  
 tctgcatctg aagctccctagc atctgggcaggt gggggccaaag aatataggttc tctgcatctga 430  
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 aagtaaaccttc aatctgattc aactgattga cctctgttgtg cttaagctctgac atctccaacca 550  
 tgaacaacact tgttcaaatc cttgaacaaatg aatatgaagct caattgtgcac atggaattcaa 610

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	toocacacca	tcgatcatag	caccacctat	cagcactgaa	aactottttg	cattaaggga	670
	toattgcaag	agcagcgtga	ctgacattat	gaaggcctgt	actgaagaca	gcaagctgtt	730
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	gatagtgttt	cagtgctggc	atattttgga	attctgcaac	ttcatggagt	gcaataatac	850
5	tgtatagctt	tcoccaacct	ccacaaaato	aocaggttaa	tgtgtgtgtg	tgtttttttt	910
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	attgagttac	aatttgattt	tttttccaaa	gatgtctgtt	aaatctgttg	tgtttttata	1030
	tgaatatattg	ttttttatag	tttaaaattg	atcctttggg	aatccagttg	aagttcccaa	1090
	atactttata	agagttttat	agacatctct	aatttggcca	tgtccagttt	atacagttta	1150
10	caaaatatag	cagatgcaag	attatggggg	aaactctata	ttcagagtac	tcataaaatt	1210
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	1						
	tgg acc aag tac cag ctg ttc ctg gcc ggg ctc atg ctt gtt acc gcc						104
	Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val Thr Gly						
	5 10 15						
30	tcc atc aac aag ctc tcg gca aaa tgg gcg gac aat ttc atg gcc gag						152
	Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met Ala Glu						
	20 25 30						
	ggc tgt gga ggg agc aag gag cac age ttc cag cat ccc ttc ctc cag						200
	Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe Leu Gln						
35	35 40 45 50						

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248	Ala Val Gly Met Phe Leu Gly Gln Phe Ser Cys Leu Ala Ala Phe Tyr	55	60	65	296
	gca gtc ggc atg ttc ctg gga gaa ttc tcc tgc ctg gct gac ttc tac				
5	ctc ctc cga tgc aga gct gca ggg caa tca gaa tcc agc gta gac ccc				
	Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val Asp Pro				
	70	75	80		
344	caag caag ccc ttc aac cct ctt ctc atc ccc cca ggc ctc ggt gac				
	Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu Cys Asp				
	85	90	95		
10	atg aca ggg aac agc ctc atg tat gtc gct ctg aac atg acc agt gcc				
	Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr Ser Ala				
	100	105	110		
440	tcc agc ttc cag atg ctg cgg ggt gca gtc atc ata ttc act ggc ctg				
	Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Phe Thr Gly Leu				
	115	120	125		
15	tcc tcc gtc ggc ttc ctg ggc cgg agc ctg gtc agc cag tgc ctg				
	Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln Trp Leu				
	135	140	145		
536	ggc atc cta gcc aac atc ggc ggc ctg gtc gtc gtc ggc ctg gac				
	Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Gly Leu Ala Asp				
	150	155	160		
584	ctc ctg agc cag caa gac agt caa gac atc agc gaa gtc atc aca				
	Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Gln Val Ile Thr				
	165	170	175		
632	ggg gac ctg ttc atc atc atc atc ggc caa gac atc gtc gtc atc				
	Gly Asp Leu Leu Ile Met Ala Gln Ile Val Ala Ile Gln Met				
	180	185	190		
680	gtg cta gag gag aag ttc gtc tac aaa caa aat gtc caa cca ctg cgg				
	Val Leu Gln Lys Phe Val Tyr Lys His Asn Val His Pro Leu Arg				
	195	200	205		
728	gca gtc ggc act gag ggc ctc ttc ggc ttc gtc atc ctc tcc ctg ctg				
	Ala Val Gly Thr Gln Gly Leu Phe Gly Phe Val Ile Leu Ser Leu Leu				
	215	220	225		
776	ctg gtc ccc atg tac tac atc ccc ggc tcc atc agc gga aac cct				
	Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly Asn Pro				
	35				

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	230	235	240	
	cgt ggg aca ctg gag gat gca ttg gac gcc ttc tgc cag gtg ggc cag			824
	Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val Gly Gln			
	245	250	255	
5	cag ccg ctc att gcc gtg gca ctg ctg ggc aac atc agc agc att gcc			872
	Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser Ile Ala			
	260	265	270	
	ttc ttc aac ttc gca ggc atc agc gtc acc aag gaa ctg agc gcc acc			920
	Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser Ala Thr			
10	275	280	285	290
	acc cgc atg gtg ttg gac age ttg cgc acc gtt gtc atc tgg gca ctg			968
	Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp Ala Leu			
	295	300	305	
	agc ctg gca ctg ggc tgg gag gcc ttc cat gca ctg cag atc ctt ggc			1016
15	Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile Leu Gly			
	310	315	320	
	ttc ctc ata ctc ctt ata ggc act gcc ctc tac aat ggg cta cac cgt			1064
	Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu His Arg			
	325	330	335	
20	ccg ctg ctg ggc cgc ctg tcc agg ggc cgg ccc ctg gca gag gag agc			1112
	Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu Glu Ser			
	340	345	350	
	gag cag gag aga ctg ctg ggt ggc acc cgc act ccc atc aat gat gcc			1160
	Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn Asp Ala			
25	355	360	365	370
	agc tgaggttccc tggaggttcc tactgccacc cgggtgetcc ttctccc			1210
	Ser			
	tgagactgag gccacacagg ctggtgggcc ccgaatgcc tatccccaag gctcaccc			1270
30	gtcccctccc tgcagaaacc ccagggcagc tgtgccaca gaagataaca acacccaagt			1330
	ctctttttc tcaataccac ctgcagggtg gtgttaccga gcccccacaa gctgagtg			1390
	agtggcagac ctacagctctc tggaccctc ctacagcact agagctaaat catgaagttg			1450
	aattgtagga atttaccacc gtatgttata tgaatcataa actagattat cat			1503
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	102	tgg gca gct cgg ctc tac ttc tat ggt att atc gct aac tcc atc tac TTP Ala Ala Ileu Ileu Tyr phe Tyr gly ile ile Ileu Asn Ser Ile Tyr 20
	15	cag tgc cct gag cac agt caa cgg aca act cgg ggc gtc gat ggg aag Gln Cys Pro Gln His Ser gln Ileu Thr Thr Ileu Val Asp Gly Iys 30 25
	20	gag ttc cca gag gtc cac tgg ggc cag tgg tac ttc atc gca ggg gca Gln Phe Pro Gln Val His Ileu Gly Gln TTP Tyr Phe Ile Ala Gly Ala 40 45 50
	246	gct ccc acc acc aag gag tgg gca act ttc gac cct gtc gac aac atc Ala Pro Thr Iys Gln Gln Ileu Ala Thr Phe Asp Pro Val Asp Asn Ile 55 60 65
25	294	gta ttc aat atg gct ggc tct ggc ccg atg cag ttc cac ctc cgt Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met Gln Ileu His Ileu Arg 70 75 80 85
	340	gct acc atc cgg atg tgaagtggaaa gatgggctct gctggccccg g Ala Thr Ile Arg Met 90
30	400	aaatcgatctc accaacctcgac tgaagggagagc aacagatctcca gaaactgaaag aatgaaagatcag agctcctcttcc ccaggtctcaatga tcaatgctgaa tggaaagaaagtc 460 520 580 640 700
		cgaggtcttccc agtcctcaaat cctcctcaaacac atccctcccgga aaaaagtgtgtgtg gaggtacaaatga agtccctctgac ttcctctggcccg gaactcccaaaa ccttccatctaat gaccccaaaagat gtcctcctgaac tggaaacctgtttaa cttccatctcaag gacttccaaagc tccaaagctccc

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	actcaagata ataaagataa tttttcaatc ctc	733
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	tgggtgttgc ccaccccggg ccgcgtgagt ggggcccac gcagctccc gcaatcogtg	180
15	ggccaaacttg gccaaagcac tctgtccggg gagcgggtgt tgcggggggg gagtacggg	240
	caactgcgat gcggagctcc aaattcaaac agctgtttc agaggtcggg gggcggggcg	300
	actggtagca gctggggcta ggagaggctt tctctaggag gcggccgctc gggagcc	357
20	atg gtg gac cgg ggc oot ctg etc acc tog gcc atc atc ttc tac ctg	405
	Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu	
	1 5 10 15	
	gcc atc ggg gog gcg atc ttc gaa gtg ctg gag gag cca cac tgg aag	453
	Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys	
25	20 25 30	
	gag gcc aag aaa aac tac tac aca cag aag ctg cat ctg etc aag gag	501
	Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu	
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	ttc ccg tgc ctg ggt cag gag ggc ctg gac aag atc cta gag gtg gta	549
30	Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val	
	50 55 60	
	tct gat gct gca gga cag ggt gtg gcc atc aca ggg aac cag acc ttc	597
	Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe	
	65 70 75 80	
35	aac aac tgg aac tgg ccc aat gca atg att ttt gca gcg acc gtc att	645

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	Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val	
	275 280 285	
	aac atc ttc agc ttt ctt tcc aag aag gaa gag acc tac aac gac ctc	1269
5	Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu	
	290 295 300	
	atc aag cag atc ggg aag aag gcc atg aag aca agc ggg ggt ggg gag	1317
	Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu	
	305 310 315 320	
10	acg ggc ccg ggc cca ggg ctg ggg cct caa ggc ggt ggg ctc cca gca	1365
	Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala	
	325 330 335	
	ctg ccc cct tcc ctg gtg ccc ctg gta gtc tac tcc aag aac cgg gtg	1413
	Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val	
15	340 345 350	
	ccc acc ttg gaa gag gtg tca cag aca ctg agg agc aaa ggc cac gta	1461
	Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val	
	355 360 365	
	tca agg tcc cca gat gag gag gct gtg gca cgg gcc cct gaa gac agc	1509
20	Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser	
	370 375 380	
	tcc cct gcc ccc gag gtg ttc atg aac cag ctg gac cgc atc agc gag	1557
	Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu	
	385 390 395 400	
25	gaa tgc gag cca tgg gac gcc cag gac tac cac cca ctc atc ttc cag	1605
	Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln	
	405 410 415	
	gac gcc agc atc acc ttc gtg aac acg gag gct ggc ctc tca gac gag	1653
	Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu	
30	420 425 430	
	gag acc tcc aag tcc tgg cta gag gac aac ttg gca ggg gag gag agc	1701
	Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser	
	435 440 445	
	ccc cag cag ggg gct gaa gcc aag gcg ccc ctg aac atg ggc gag ttc	1749
35	Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe	

450 455 460

1797

Pro Ser Ser Ser Gln Ser Thr Phe Thr Ser Thr Gln Ser Gln Leu Ser

465	470	475	480
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b6  
b7C

gty cct tac gaa cay ctg atg gat gag tac aac aag gctaac cc  
1845

Val Pro Tyr Glu Gln Leu Met Asn Gln Tyr Asn Lys Ala Asn Ser Pro

485 490 495

၁၈၉၆ ခုနှစ် ဇန်နဝါရီလ ၁ ရက်နေ့တွင် ရန်ကုန်မြို့တွင် ဖွားမြင်သည်။

THE LATE

၀၄၆၇    နှစ်နှစ်သဘာဝ    ဝန်ပိုင်ပိုင်ခွင့်    နှစ်သဘာဝခွင့်    နှစ်သဘာဝခွင့်    နှစ်သဘာဝခွင့်    နှစ်သဘာဝခွင့်    နှစ်သဘာဝခွင့်

[illegible][illegible]

0៩17      ៩៩៩៩៩៩៩៩ ៩៩៩៩៩៩៩៩៩ ៩៩៩៩៩៩៩៩៩ ៩៩៩៩៩៩៩៩៩ ៩៩៩៩៩៩៩៩៩ ៩៩៩៩៩៩៩៩៩

0617 282282226 222266668 622622226 666666222 662266666 666666666 0

0577 16622226 22226662 16622226 16622226 16622226 16622226

0157 26262626 26666666 26266666 26666666 62262626 26662626

၁/၆၃ ၆၆၃၆၃၆၇၃၃ ၃၃၇၃၆၃၃၆၃ ၃၃၆၆၆၇၃၆၇၆ ၆၇၃၆၇၃၇၃၃၇ ၃၆၃၃၃၃၆၃၆ ၆၇၃၃၆၆၆၆-၆

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0613      nnnnnn66aa   6666nnnnaa   n6aa6666nn   nnaa6666nn   6666n6an6n   66n6a6n666

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[illegible]

0403 5570067006 5570067006 5570067006 5570067006 5570067006 5570067006

0017

0018

[illegible]

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[illegible]

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3150

[illegible]

1575

7330

3 390

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	gcagtggggc cagagcccac ctcccaca tgtagaagaca gtgatgggca cgtgcccaca	3570
	ccccacttc tctagccgtt tgcagaggcc gccaccagc aggggacctga aaaggagcag	3630
5	cctgtattt ttctgtgaaa tgttttaatg aaccatgttg ttgtgggttg tectggcacc	3690
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	gat tct aag cgt gga gag gcc cgg ttc gct cag cgt atc gac cgg act	101
	Asp Ser Lys Arg Gly Glu Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr	
	15 20 25	
	egg gag aag ctg aca ccc gag caa ctg cat tcc atg cgg cag gcg gag	149
25	Arg Glu Lys Leu Thr Pro Glu Gln Leu His Ser Met Arg Gln Ala Glu	
	30 35 40	
	ctt gcc cag tgg cag aag gtc cta cca cgg cgg cga acc cgg aac atc	197
	Leu Ala Gln Trp Gln Lys Val Leu Pro Arg Arg Arg Thr Arg Asn Ile	
	45 50 55	
30	gtg acc gcc cta gcc atc ggg gcc ctg gtg ttg gct att tat ggt tac	245
	Val Thr Gly Leu Gly Ile Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr	
	60 65 70	
	acc ttc tac tcg att tcc cag gag cgt ttc cta gat gag cta gaa gac	293
	Thr Phe Tyr Ser Ile Ser Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp	
35	75 80 85 90	

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341	gag gcc aac gct gcc cga gcc cga gct cta gca agc gca ggc tca ggc tcc	95	100	105	400
	gln ala lys ala arg ala arg ala leu ala ser gln ala ser				410
	taactgga tgggtataga tcaatgtccaa ccctcggag ccctccaa tggtagatga				420
5	tgcacacatga ccctgtcagaa attgaaatcc tctcacaaac ttgttggcct tctcaaac				430
	cttgaaaccgt gattgaagccc aagaaaccaa gaaacttaagc atttggccaa ttccaaagaa				440
	acgaaacctt gccacatgca caactgtcgt gtacaaatgaa ttgaagccctt ctgtcaagctt				450
	gttcccttctgt ttgaagagtg ttgcattgcaac cgttggccttt ccnaaagctt ctgaacttctgt				460
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	ile ile thr ser val gln leu ala gln lys ser				210
	ile thr ser val gln leu ala gln lys ser				220
	ile thr ser val gln leu ala gln lys ser				230
	ile thr ser val gln leu ala gln lys ser				240
35	atc atc acc tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca	40	45	50	257
	ile thr ser val gln leu ala gln lys ser				260
	ile thr ser val gln leu ala gln lys ser				270
	ile thr ser val gln leu ala gln lys ser				280
	ile thr ser val gln leu ala gln lys ser				290
40	atc atc acc tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca	45	50	55	305
	ile thr ser val gln leu ala gln lys ser				310
	ile thr ser val gln leu ala gln lys ser				320
	ile thr ser val gln leu ala gln lys ser				330
	ile thr ser val gln leu ala gln lys ser				340
	ile thr ser val gln leu ala gln lys ser				350
	ile thr ser val gln leu ala gln lys ser				360
	ile thr ser val gln leu ala gln lys ser				370
	ile thr ser val gln leu ala gln lys ser				380
	ile thr ser val gln leu ala gln lys ser				390
	ile thr ser val gln leu ala gln lys ser				400
	ile thr ser val gln leu ala gln lys ser				410
	ile thr ser val gln leu ala gln lys ser				420
	ile thr ser val gln leu ala gln lys ser				430
	ile thr ser val gln leu ala gln lys ser				440
	ile thr ser val gln leu ala gln lys ser				450
	ile thr ser val gln leu ala gln lys ser				460
	ile thr ser val gln leu ala gln lys ser				470
	ile thr ser val gln leu ala gln lys ser				480
	ile thr ser val gln leu ala gln lys ser				490
	ile thr ser val gln leu ala gln lys ser				500

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Ser Met Cys Leu Leu Phe Leu Trp Lys Lys Tyr Gln Pro Tyr Lys Val  
 55 60 65 70  
 ata aaa cag aaa cta gaa ggc agg cca gaa aca gaa tac agg aaa gct 353  
 Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu Thr Glu Tyr Arg Lys Ala  
 5 75 80 85  
 caa aca ttt tca ggc cat gaa gat gct ctg gat gac ttc gga ata tat 401  
 Gln Thr Phe Ser Gly His Glu Asp Ala Leu Asp Asp Phe Gly Ile Tyr  
 90 95 100  
 gaa ttt gtt gct ttt cca gat gtt tct ggt gtt tcc agg atc cca agc 449  
 10 Glu Phe Val Ala Phe Pro Asp Val Ser Gly Val Ser Arg Ile Pro Ser  
 105 110 115  
 agg tct gtt cca gcc tct gat tgt gta tgg ggg caa gat ttg cac agt 497  
 Arg Ser Val Pro Ala Ser Asp Cys Val Ser Gly Gln Asp Leu His Ser  
 120 125 130  
 15 aca gtg tat gaa gtt att cag cac atc cct gcc cag cag caa gac cat 545  
 Thr Val Tyr Glu Val Ile Gln His Ile Pro Ala Gln Gln Gln Asp His  
 135 140 145 150  
 oca gag tgaacttcca tgggctaaac agtacattcg agtgaaatc tgaagaac 600  
 Pro Glu  
 20  
 attttaaggaa aaaacagtg aaagtatat taatctggaa tcaagtgaaga aaccaagacc 660  
 aacacotctt actcattatt cctttacatg cagaatagag gcattttatgc aaattgaact 720  
 gcagggtttt cagcatatac acaatgtctt gtgcaacaga aaaacatggt ggggaaatat 780  
 tctcagtgag agagctgttc tcatgctgac ggggagaacg aaagtgcag ggggttcttc 840  
 25 ataagttttg tatgaaatat ctctacaac ctcaattagt tctactctac actttcacta 900  
 toatcaacac tgagactatc ctgtctcaac tacaattgtg gaaactttac attgttcgat 960  
 ttttcagcag actttgtttt attaaatttt tattagtgtt aagaatgcta aagtttcaat 1020  
 tttatttoca aatttctatc ttgttatttg tacaacaaag taataaggat ggttgcaca 1080  
 aaaacaaaac tatgccttct ctttttttcc aatcacacgt agtatttttg agaagaattg 1140  
 30 tgaacactta aggaaatgac tattaaagtc ttatttttat ttttttcaag gaaagatgga 1200  
 ttcaaatata ttattctgtt ttgtctttt 1229  
 <210> 91  
 <211> 358  
 35 <212> PRT

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<213> Homo sapiens

<400> 91

Met Ala Pro Gln Asn Leu Ser Thr Phe Cys Leu Leu Leu Tyr Leu  
1 5 10 15

Ile Gly Ala Val Ile Ala Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val  
20 25 30

Pro Arg Ser Ala Ser Ile Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu  
35 40 45

Ala Leu Gln Leu His Pro Asp Asn Pro Asp Asp Pro Gln Ala Gln  
50 55 60

Gln Lys Phe Gln Asp Leu Gly Ala Ala Tyr Gln Val Leu Ser Asp Ser  
65 70 75 80

Gln Lys Arg Lys Gln Tyr Asp Thr Tyr Gly Gln Gln Gly Leu Lys Asp  
85 90 95

Gly His Gln Ser Ser His Gly Asp Ile Phe Ser His Phe Phe Gly Asp  
100 105 110

Phe Gly Phe Met Phe Gly Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile  
115 120 125

Pro Arg Gly Ser Asp Ile Ile Val Asp Leu Gln Val Thr Leu Gln Gln  
130 135 140

Val Tyr Ala Gly Asn Phe Val Gln Val Val Arg Asn Lys Pro Val Ala  
145 150 155 160

Arg Gln Ala Pro Gly Lys Arg Lys Cys Asn Cys Arg Gln Gln Met Arg  
165 170 175

Thr Thr Gln Leu Gly Pro Gly Arg Phe Gln Met Thr Gln Val Val  
180 185 190

Cys Asp Gln Cys Pro Asn Val Lys Leu Val Asn Gln Arg Thr Leu  
195 200 205

Gln Val Gln Ile Gln Pro Gly Val Arg Asp Gly Met Tyr Pro Phe  
210 215 220

Ile Gly Gln Gly Gln Pro His Val Asp Gly Gln Pro Gly Asp Leu Arg  
225 230 235 240

Phe Arg Ile Lys Val Lys His Pro Ile Phe Gln Arg Arg Gly Asp  
245 250 255

35

30

25

20

15

10

5

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Asp Leu Tyr Thr Asn Val Thr Ile Ser Leu Val Glu Ser Leu Val Gly  
                   260                  265                  270  
 Phe Glu Met Asp Ile Thr His Leu Asp Gly His Lys Val His Ile Ser  
                   275                  280                  285  
 5 Arg Asp Lys Ile Thr Arg Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu  
                   290                  295                  300  
 Gly Leu Pro Asn Phe Asp Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile  
                   305                  310                  315                  320  
 Thr Phe Asp Val Asp Phe Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg  
                   325                  330                  335  
 10 Glu Gly Ile Lys Gln Leu Leu Lys Gln Gly Ser Val Gln Lys Val Tyr  
                   340                  345                  350  
 Asn Gly Leu Gln Gly Tyr  
                   355  
 15  
 <210> 92  
 <211> 226  
 <212> PRT  
 <213> Homo sapience  
 20  
 <400> 92  
 Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser Asn Ser Cys Cys  
           1                  5                  10                  15  
 Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr  
                   20                  25                  30  
 25 Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala  
                   35                  40                  45  
 Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe  
           50                  55                  60  
 30 Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu  
           65                  70                  75                  80  
 Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln  
                   85                  90                  95  
 Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe  
 35                  100                  105                  110

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35	85	Ile Tyr Arg His Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu	95
		Arg Tyr Pro Asp Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro	80
30	50	Xaa Gly Tyr Arg Arg Val Phe Glu Tyr Met Arg Val Ile Ser Gln	60
		Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser	45
		Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Lys	30
		Met Arg Leu Leu Leu Leu Leu Leu Val Ala Ser Ala Met Val Arg	15
25	5	<400> 93	
		<213> Homo sapience	
		<212> FRT	
		<211> 195	
20	93	<210> 93	
		Ser Ala	225
		Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro Tyr Val	210
		Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Tyr Asp	205
15	215	Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu	195
		Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu Ile Ser Cys Val	180
		Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Ile Ile Leu Leu	165
		Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe Pro Tyr Arg Asp	150
10	135	Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile Tyr Pro Asn Ser	145
		Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu	130
		Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Tyr Asp	115
		Met Arg Leu Leu Leu Leu Leu Leu Val Ala Ser Ala Met Val Arg	100
5	125	<400> 93	
		<213> Homo sapience	
		<212> FRT	
		<211> 195	



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Ile Gly Leu Ile Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met  
                   100                                  105                                  110  
 Gln Ala Pro Ser Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala  
                   115                                  120                                  125  
 5 Cys Met Met Val Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met  
                   130                                  135                                  140  
 Ser Thr Gly Ala Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser  
                   145                                  150                                  155                                  160  
 Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile  
 10                                   165                                  170                                  175  
 Leu Asp Asn Glu Met Lys Leu Asn Val His Met Asp Ser Ile Pro His  
                   180                                  185                                  190  
 His Arg Ser  
                   195  
 15  
 <210> 94  
 <211> 339  
 <212> PRT  
 <213> Homo sapiens  
 20  
 <400> 94  
 Met Asn Trp Glu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu  
                   1                                  5                                  10                                  15  
 Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu  
 25                                   20                                  25                                  30  
 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu  
                   35                                  40                                  45  
 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu  
                   50                                  55                                  60  
 30 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser  
                   65                                  70                                  75                                  80  
 Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu  
                   85                                  90                                  95  
 Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu  
 35                                   100                                  105                                  110

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Thr Asp Thr Gly Ser His Glu Ala Thr Lys Ala Val Leu Glu  
125 120

Phe Arg Ile Asp Ile Leu Val Asn Gly Met Ser Glu Arg  
130 135

Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu  
145 150 155

Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His  
160 170 175

Met Ile Glu Arg Lys Glu Gly Lys Ile Val Thr Val Asn Ser Ile Leu  
180 185 190

Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His  
195 200 205

Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr  
210 215 220

Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Glu Ser Asn  
225 230 235

Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn  
240 250 255

Asn Gly Asp Glu Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu  
260 265 270

Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Thr Ile Ser Glu  
275 280 285

Gln Pro Phe Leu Leu Val Thr Tyr Leu Thr Glu Tyr Met Pro Thr Thr  
290 295 300

Ala Thr Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe  
305 310 315 320

Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr  
325 330 335

Lys His Asp

5

10

15

20

25

30

35

&lt;210&gt; 95

&lt;211&gt; 487

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

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<400> 95

Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys  
 1 5 10 15

Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro  
 5 20 25 30

Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val  
 35 40 45

Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser  
 50 55 60

Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu  
 10 65 70 75 80

Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe  
 85 90 95

Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu  
 15 100 105 110

Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala  
 115 120 125

Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser  
 130 135 140

Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu  
 20 145 150 155 160

Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val  
 165 170 175

Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala  
 25 180 185 190

Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile  
 195 200 205

Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile  
 210 215 220

Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val  
 30 225 230 235 240

Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu  
 245 250 255

Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala  
 35 260 265 270

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lys gln ser pro ile val lys ile leu lys phe gly trp phe pro

275

280

285

ile ile leu ala met val ile ser ser phe gly ile leu ser

290

295

300

lys thr val ser lys gln gln tyr lys gly met ala ile phe thr pro

305

310

315

val ile cys gly val gly gly am leu val ala ile gln thr ser arg

325

330

335

ile ser thr tyr leu his met trp ser ala pro gly val leu pro leu

340

345

350

gln met lys lys phe trp pro am pro cys ser thr phe thr ser

355

360

365

gln ile am ser met ser ala arg val leu leu leu val val pro

370

375

380

gly his leu ile phe phe tyr ile ile tyr leu val gln gly ser

385

390

395

val ile am ser gln thr phe val leu tyr leu leu ala gly ile

405

410

415

ile gln val thr ile leu leu tyr leu ala gln val met val arg leu

420

425

430

thr trp his gln ala leu asp pro asp am his cys ile pro tyr leu

435

440

445

thr gly leu gly asp leu leu gly thr gly leu leu ala leu cys phe

450

455

460

phe thr asp trp leu leu lys ser lys ala gln leu gly gly ile ser

465

470

475

gln leu ala ser gly pro pro

485

35

&lt;400&gt; 96

30

&lt;210&gt; 96

&lt;211&gt; 393

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

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Met Arg Thr Leu Phe Asn Leu Leu Trp Leu Ala Leu Ala Cys Ser Pro  
 1 5 10 15  
 Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala Ala Ser Lys  
 20 25 30  
 5 Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp Lys Pro Val Gln Asp Arg  
 35 40 45  
 Gly Leu Val Val Thr Asp Leu Lys Ala Glu Ser Val Leu Leu Glu His  
 50 55 60  
 Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp Arg His Phe Ala Gly Asp  
 10 65 70 75 80  
 Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr Asp Val Thr  
 85 90 95  
 Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val Trp Leu Gln  
 100 105 110  
 15 Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Val Thr Gly Leu His Asp  
 115 120 125  
 Val Asp Gln Gly Trp Met Arg Ala Val Arg Lys His Ala Lys Gly Leu  
 130 135 140  
 His Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr Asp Asp Phe  
 20 145 150 155 160  
 Arg Asn Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu Ser Lys Thr  
 165 170 175  
 Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe Val Val Glu  
 180 185 190  
 25 Val Trp Asn Gln Leu Leu Ser Gln Lys Arg Val Gly Leu Ile His Met  
 195 200 205  
 Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu Leu Ala Leu  
 210 215 220  
 Leu Val Ile Pro Pro Ala Ile Thr Pro Gly Thr Asp Gln Leu Gly Met  
 30 225 230 235 240  
 Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Val Leu Asp Gly Phe  
 245 250 255  
 Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala His Gln Pro Gly Pro Asn  
 260 265 270  
 35 Ala Pro Leu Ser Trp Val Arg Ala Cys Val Gln Val Leu Asp Pro Lys

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35	gin gln val thr leu gln pro gly gln tyr ile thr lys val phe val 95 leu gly asp ser trp asp val lys leu gly ala leu gly gly asn thr 80 leu arg val ser val gly leu leu leu val lys ser val gln val lys 65 leu leu gly gly pro thr trp ala gly lys met tyr gly pro gly gly 45 gly lys tyr phe ser thr thr gln asp tyr asp his gln ile thr gly 30 leu leu gly gly pro thr trp ala gly lys met tyr gly pro gly gly 35 leu leu gly gly pro thr trp ala gly lys met tyr gly pro gly gly 25 pro gly met his arg pro gln ala met leu leu leu thr leu ala 1 met trp arg val pro gly thr thr arg arg pro val thr gly gln ser 15 <210> 97 <400> 97
20	<210> 97 <211> 196 <212> PRT <213> Homo sapiens
15	gly leu asp tyr phe tyr asp leu leu 390 leu ala arg gln leu gly val gly val ser ile trp gln leu gly gln 370 leu ala arg gln leu gly val gly val ser ile trp gln leu gly gln 385 his val val phe tyr pro thr leu lys ser leu gln val arg leu gln 355 gln ala ser gln his phe phe gln tyr lys lys ser arg ser gly arg 340 tyr ile gln thr leu lys asp his arg pro arg met val trp asp ser 325 tyr ile gln thr leu lys asp his arg pro arg met val trp asp ser 305 asp tyr ala thr ser lys ser lys ile leu leu gly leu asn phe tyr gly met 290 ser lys trp arg ser lys ile leu leu gly leu asn phe tyr gly met 275 ser lys trp arg ser lys ile leu leu gly leu asn phe tyr gly met 285
10	his val val phe tyr pro thr leu lys ser leu gln val arg leu gln 360 gln ala ser gln his phe phe gln tyr lys lys ser arg ser gly arg 345 tyr ile gln thr leu lys asp his arg pro arg met val trp asp ser 330 tyr ile gln thr leu lys asp his arg pro arg met val trp asp ser 315 asp tyr ala thr ser lys ser lys ile leu leu gly leu asn phe tyr gly met 300 ser lys trp arg ser lys ile leu leu gly leu asn phe tyr gly met 285
5	asp tyr ala thr ser lys ser lys ile leu leu gly leu asn phe tyr gly met 300 ser lys trp arg ser lys ile leu leu gly leu asn phe tyr gly met 285 ser lys trp arg ser lys ile leu leu gly leu asn phe tyr gly met 275 ser lys trp arg ser lys ile leu leu gly leu asn phe tyr gly met 285

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100 105 110  
 Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp  
 115 120 125  
 Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr  
 5 130 135 140  
 Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln Tyr Gln  
 145 150 155 160  
 Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu  
 165 170 175  
 10 Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala Asn Ser  
 180 185 190  
 Pro Val Gly Arg  
 195  
 15 <210> 98  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens  
 20 <400> 98  
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met Ser  
 1 5 10 15  
 Thr Asp Thr Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly Ser  
 20 25 30  
 25 Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly Ile  
 35 40 45  
 Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser  
 50 55 60  
 Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala  
 65 70 75 80  
 30 Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser  
 85 90 95  
 Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro  
 100 105  
 35

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<210> 99  
 <211> 350  
 <212> PRT  
 <213> Homo sapiens

5

<400> 99  
 Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly Pro Lys Gly Ala Pro  
 1  
 5  
 10  
 15

Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Lys Thr Pro Val Ala  
 20  
 25  
 30

Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser  
 35  
 40  
 45

Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Glu  
 50  
 55  
 60

Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln Tyr Gln Leu Leu Lys  
 65  
 70  
 75  
 80

Leu Glu Thr Asn Glu Phe Gln Glu Leu Glu Ser Lys Ile Ser Leu Ile  
 85  
 90  
 95

Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met Glu Gln Leu Lys Ser  
 100  
 105  
 110

Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Glu Ile Asn Glu  
 115  
 120  
 125

Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys Gln Asp Ile Leu Asn  
 130  
 135  
 140

Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser  
 145  
 150  
 155  
 160

Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys  
 165  
 170  
 175

Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu  
 180  
 185  
 190

Thr Asp Ser Val Gln Glu Leu Asn Lys Ile Gln Lys Val Gln Lys  
 195  
 200  
 205

Asn Thr Val Lys Asn Ile Gly Asp Leu Ser Ser Ile Asp Arg  
 210  
 215  
 220

Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn Ser Gln Arg Ile Asn  
 225  
 230  
 235

35

30

25

20

15

10



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225                      230                      235                      240  
 Ser Val Lys Lys Thr Leu Thr Glu Leu Lys Ser Asp Phe Asp Lys His  
                          245                      250                      255  
 Thr Asp Arg Phe Leu Ser Leu Glu Gly Asp Arg Ala Lys Val Leu Lys  
 5                      260                      265                      270  
 Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys Val Tyr Asn Leu Lys  
                          275                      280                      285  
 Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn Asp Leu Thr Leu Arg  
                          290                      295                      300  
 10    Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Glu Lys Glu Ile Ala  
                          305                      310                      315                      320  
 Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile Val Gln Ala Glu Ile  
                          325                      330                      335  
 Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser Asp Met Asn  
 15                      340                      345                      350  
  
 <210> 100  
 <211> 107  
 <212> PRT  
 20    <213> Homo sapience  
  
 <400> 100  
 Met Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu  
                          1                      5                      10                      15  
 25    Thr Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser  
                          20                      25                      30  
 Ile Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu  
                          35                      40                      45  
 Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val  
 30                      50                      55                      60  
 Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Ser Leu Met Ser Leu  
                          65                      70                      75                      80  
 Leu Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly  
                          85                      90                      95  
 35    Arg Pro Ala Gly Gly Ala His Leu Cys Ala Ala

105

<210> 101  
<211> 1074  
<212> DNA  
<213> Homo Sapiens

<400> 101

[illegible][illegible][illegible][illegible][illegible]

<210> 102  
<211> 678  
<212> DNA  
<213> Homo Sapiens

[illegible]

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Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Gln Leu His Pro  
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gac cgg aac cct gat gat cca cca gcc cag gag aac ttc cag gat ctg 367  
Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Lys Phe Gln Asp Asp Leu  
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75 80 85  
gat acc tat ggt gaa gaa gaa cta aaa gat ggt cat cag agc tcc cat 463  
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	Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile Pro Arg Gly Ser Asp Ile			
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	Ile Val Asp Leu Glu Val Thr Leu Glu Glu Val Tyr Ala Gly Asn Phe			
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	Val Glu Val Val Arg Asn Lys Pro Val Ala Arg Gln Ala Pro Gly Lys			
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	cgg aag tgc aat tgt cgg caa gag atg cgg acc acc cag ctg ggc cct			703
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	ggg cgc ttc caa atg acc cag gag gtg gtc tgc gac gaa tgc cct aat			751
	Gly Arg Phe Gln Met Thr Gln Glu Val Val Cys Asp Glu Cys Pro Asn			
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	Val Lys Leu Val Asn Glu Glu Arg Thr Leu Glu Val Glu Ile Glu Pro			
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	ggg gtg aga gac ggc atg gag tac ccc ttt att gga gaa ggt gag cct			847
	Gly Val Arg Asp Gly Met Glu Tyr Pro Phe Ile Gly Glu Gly Glu Pro			
25	215	220	225	230
	cac gtg gat ggg gag cct gga gat tta cgg ttc cga atc aaa gtt gtc			895
	His Val Asp Gly Glu Pro Gly Asp Leu Arg Phe Arg Ile Lys Val Val			
	235	240	245	
	aag cac cca ata ttt gaa agg aga gga gat gat ttg tac aca aat gtg			943
30	Lys His Pro Ile Phe Glu Arg Arg Gly Asp Asp Leu Tyr Thr Asn Val			
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	aca atc tca tta gtt gag tca ctg gtt ggc ttt gag atg gat att act			991
	Thr Ile Ser Leu Val Glu Ser Leu Val Gly Phe Glu Met Asp Ile Thr			
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5	295 300 305 310		
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	Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu	
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	Pro Tyr Arg Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu	
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	att att ctt ctg ttt att agc att atc ttg act ttt aag ggt tac ttg	769
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	Pro Pro Tyr Asp Ala Thr Val Asn Gly Ala Ala Iys Glu Pro Pro	210	220
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<212> DNA

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<214> 113

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&lt;400&gt; 113

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	acg ggg ccg ctg ctc aag ttc cag att tgt gtt tcc tga ggt tat agg	198
15	Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gly Tyr Arg	
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	egg gtg ttt gag gag tac atg cgg gtt att agc cag cgg tac cca gac	246
	Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp	
	55 60 65	
20	atc cgc att gaa gga gag aat tac ctc cct caa cca ata tat aga cac	294
	Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro Ile Tyr Arg His	
	70 75 80	
	ata gca tct ttc ctg tca gtc ttc aaa cta gta tta ata ggc tta ata	342
	Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gly Leu Ile	
25	85 90 95 100	
	att gtt ggc aag gat cct ttt gct ttc ttt ggc atg caa gct cct agc	390
	Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met Gln Ala Pro Ser	
	105 110 115	
	atc tgg cag tgg ggc caa gaa aat aag gtt tat gca tgt atg atg gtt	438
30	Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala Cys Met Met Val	
	120 125 130	
	ttc ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca	486
	Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met Ser Thr Gly Ala	
	135 140 145	
35	ttt gag ata act tta aat gat gta cct gtg tgg tct aag ctg gaa tct	534

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Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser Lys Leu Glu Ser  
 150 155 160  
 ggt cac ctt cca tcc atg caa cct gtt caa att ctt gac aat gaa  
 582  
 Gly His Leu Pro Ser Met Glu Glu Leu Val Glu Ile Leu Asp Asn Glu  
 170 175 180  
 atg aag ctc aat gtc gat atg tca atc cca cca cat cga tca  
 627  
 Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser  
 185 190 195

10 tng caccacat cagacatgaa aactccttgg catlaagggaa tcatcgaag  
 680  
 740 agcagcgtgga ctgacatlat gaagagcctgt acctgaagacaa gcaagcctgtc agtacaagacc  
 800  
 860 cagtcctcctgg aatctctggaa atctctgcacaa ttcactggaggt gcaattaatatc tgcataagcctc  
 920  
 980 tcccccacccctc ccaacaaatcc acccaagttcaa tgggtgtgtgtgtc tgtttttttttc tttaaggttaa  
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 118 gacctctgtgt cgggcctgtct tcttccccccc gaggctggggc tggcgcgggcg ca atg aac  
 118  
 1  
 Met Asn

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	tgg gag ctg ctg ctg tgg ctg ctg gtg ctg tgc gcg ctg ctc ctg ctc	166
	Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu	
	5 10 15	
	ttg gtg cag ctg ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta	214
5	Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu	
	20 25 30	
	cta tgg gcc gag tgg cag gga cga cgc cca gaa tgg gag ctg act gat	262
	Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp	
	35 40 45 50	
10	atg gtg gtg tgg gtg act gga gcc tcg agt gga att ggt gag gag ctg	310
	Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu	
	55 60 65	
	gct tac cag ttg tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga	358
	Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg	
15	70 75 80	
	aga gtg cat gag ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc	406
	Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly	
	85 90 95	
	aat tta aaa gaa aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac	454
20	Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp	
	100 105 110	
	act ggt tcc cat gaa gcg gct acc aaa gct gtt ctc cag gag ttt ggt	502
	Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu Phe Gly	
	115 120 125 130	
25	aga atc gac att ctg gtc aac aat ggt gga atg tcc cag cgt tct ctg	550
	Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg Ser Leu	
	135 140 145	
	tgc atg gat acc agc ttg gat gtc tac aga aag cta ata gag ctt aac	598
	Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu Leu Asn	
30	150 155 160	
	tac tta ggg acg gtg tcc ttg aca aaa tgt gtt ctg cct cac atg atc	646
	Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile	
	165 170 175	
	gag agg aag caa gga aag att gtt act gtg aat agc atc ctg ggt atc	694
35	Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile	

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742	ata tct cta cct ctc tcc att gga tac tgt gct agc aag cat gct ctc	180	185	190
195	ile ser val pro leu ser ile gly tyr cys ala ser lys his ala leu	200	205	210
190	cgg ggt ttc ttc tat ggc ctc cga aca gaa ctt gcc aca tac cca ggt	215	220	225
838	ata ata gtc tct aac att tgc cca gga cct gtc caa tca att att gtc	230	235	240
886	gag aat tcc cta gct gga gaa gtc aca aag aat ata ggc aat gga	245	250	255
934	gac cag tcc cac aag atg aca acc agt cgt cgt gtc cgg cgt atg tta	260	265	270
15	asp gln ser thr thr ser arg cys val arg leu met leu	275	280	285
20	lta tct tca gta aca tat tct tgg cca tac atg cca acc tgg gct tgg	290	295	300
1030	phe leu leu val thr tyr leu trp gln tyr met pro thr trp ala trp	305	310	315
1078	tgg ata acc aac aag atg ggg aag aaa aag att gag aac ttt aag agt	320	325	330
1126	ggt gtc gat gca gac tct cct tat tct aaa atc tta aag aca aaa cat	335	340	345
1180	gac tggaaagagc atcctgtacct ttcgaagccac tggaggggaaa aatggaaac a	350	355	360
30	asp			
35	tggaaacagac aatctctcta tga tgcctctgaa caatccaaagaa ctatcttgty gttcttaacct	1240	1245	1250
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 Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys  
 1 5 10 15  
 cca ggg gag ctg ggg ctt cct cac ccc ctc agc aca gga gga ctc cct 151  
 Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro  
 15 20 25 30  
 gta gcc tca gaa gat gga gct ctc agg gcc cct gag agc caa agc gtg 199  
 Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val  
 35 40 45  
 acc ccc aag cca ctg gag act gag cct agc agg gag acc gcc tgg tcc 247  
 20 Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser  
 50 55 60  
 ata ggc ctt cag gtg acc gtg ccc ttc atg ttt gca ggc ctg gga ctg 295  
 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu  
 65 70 75 80  
 25 tcc tgg gcc ggc atg ctt ctg gac tat ttc cag cac tgg cct gtg ttt 343  
 Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe  
 85 90 95  
 gtg gag gtg aaa gac ctt ttg aca ttg gtg ccg ccc ctg gtg ggc ctg 391  
 Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu  
 30 100 105 110  
 aag ggg aac ctg gag atg aca ctg gca tcc aga ctc tcc aca gct gcc 439  
 Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala  
 115 120 125  
 aac act gga caa att gat gac ccc cag gag cag cac aga gtc atc agc 487  
 35 Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser

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535	agc aac ctc gcc ctc atc cag gtc cag gcc act gtc gtc ggc ctc tgc	130	135	140
	Ser Asn Leu Ala Leu Ile Gln Val Ile Gln Val Val Gln Val Leu Leu	145	150	155
583	gct gct gtc gtc gcc ctc gtc tgc gtc gtc gtc gtc gtc cga gag gaa gtc	160	165	170
	Ala Ala Val Ala Ala Leu Leu Gln Val Val Ser Arg Gln Gln Val	175	180	185
631	gat gtc gcc aag gtc gag tgc gtc gtc gtc gtc gtc gtc gtc gtc gtc gtc	190	195	200
	Asp Val Ala Ala Lys Val Gln Leu Leu Cys Ala Ser Ser Val Leu Thr Ala	205	210	215
679	ttc ctc gca gcc ttc gcc ctc ggc gtc gtc gtc gtc gtc gtc gtc gtc gtc	220	225	230
	Phe Leu Ala Ala Phe Ala Leu Gln Val Leu Met Val Cys Ile Val Ile	235	240	245
727	ggt gct cga aag ctc ggc gtc aac cca gag aac gtc gtc gtc gtc gtc gtc	250	255	260
	Gly Ala Arg Lys Leu Gln Val Asn Pro Asp Asn Ile Ala Thr Pro Ile	265	270	275
775	gca gcc aac ctc ggc gga gac ctc atc aca ctc tcc att ctc gtc tgc gtc	280	285	290
	Ala Ala Ser Leu Gln Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val	295	300	305
823	agc aac ttc ttc tac aga cac aga gat agt cgc cgc ctc ctc ctc ctc ctc	310	315	320
	Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu	325	330	335
871	gtc tgc ctc aac gct ttc gcc gct ctc gtc aac cca gtc tgc gtc gtc gtc	340	345	350
	Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala	355	360	365
919	aag cag aac cca ccc atc gtc aag atc ctc aag ttc gtc tgc ctc cca	370	375	380
	Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro	385	390	395
967	atc atc ctc gcc atc gtc atc aag agt ttc gga gga ctc atc ctc gtc agc	400	405	410
	Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gln Ile Leu Ser	415	420	425
1015	aaa aac gtc ttc tct aaa cag cag tac aaa ggc atc ggc ata ttc aac ccc	430	435	440
	Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro	445	450	455
1063	gtc ata tgc gtc gtc gtc gtc gtc gtc gtc gtc gtc gtc gtc gtc gtc	460	465	470

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	Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg	
	325 330 335	
	atc tca acc tac ctg cac atg tgg agt gca cct ggc gtc ctg ccc etc	1111
	Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu	
5	340 345 350	
	cag atg aag aaa ttc tgg ccc aac ceg tgt tct act ttc tgc acg tca	1159
	Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser	
	355 360 365	
	gaa atc aat tcc atg tca gct cga gtc ctg ctc ttg ctg gtg gtc cca	1207
10	Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Leu Val Val Pro	
	370 375 380	
	ggc cat ctg att ttc ttc tac atc atc tac ctg gtg gag ggt cag tca	1255
	Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser	
	385 390 395 400	
15	gtc ata aac agc cag acc ttt gtg gtg ctc tac ctg ctg gca ggc ctg	1303
	Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu	
	405 410 415	
	atc cag gtg aca atc ctg ctg tac ctg gca gaa gtg atg gtt cgg ctg	1351
	Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu	
20	420 425 430	
	act tgg cac cag gcc ctg gat cct gac aac cac tgc atc ccc tac ctt	1399
	Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu	
	435 440 445	
	aca ggg ctg ggg gac ctg ctc ggt act ggc ctc ctg gca ctc tgc ttt	1447
25	Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe	
	450 455 460	
	ttc act gac tgg cta ctg aag agc aag gca gag ctg ggt ggc atc tca	1495
	Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser	
	465 470 475 480	
30	gaa ctg gca tct gga cct ccc taactggggc ccgctggtcc catttgetca ttg	1550
	Glu Leu Ala Ser Gly Pro Pro	
	485	
	aatttcctct cacatcagtg ggatacagaa ttcaagtttct coettgcoag gtcottggga	1610
	tggttgaccc ctgcctctgc agtagccttt tgtgagtcgt ctaaggtagc tctcacacac	1670
35	ctcggtctgt ggggtgatac ctgagcctgc aatagagccc tgaatcaag agcatggctt	1730

35 60 65 70  
 agn cna ttc gct ggc gat gta ctg ggc tat gtc act cca tgg aac agc  
 Ser Val Val Leu Gln His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp  
 302 agt gtc gtc ctc gag cat cgc agc tac tgc tgc gca aag gcc cgg gac  
 45 50 55  
 Lys Pro Val Gln Asp Arg Gly Leu Val Thr Asp Lys Ala Gln  
 254 aag ccg gtc caa gac cgg ggt tgg gtc agc gac ctc aaa gct gag  
 30 35 40  
 Lys Lys Ala Ala Ser Lys Thr Leu Leu Gln Lys Ser Gln Phe Ser Asp  
 203 aaa aaa gcc gcc tca aag aag cty gga aag agt cag ttc tca gat  
 25 20 25  
 Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala  
 158 gcc ctg gcc tgc aag cct gtt caa act acc cty tca aag tca gat gcc  
 1 5 10  
 Met Arg Thr Leu Phe Asn Leu Leu Trp Leu  
 110 cctactctgag caacactaac atg cgg acc ctc ttc aac ctc ctc tgg ctt  
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 1790 gtaggtctgaa atcagatctgt tgcacatcgt taatgagagct gcaaggtctgc aacacgtctgt  
 1790

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	Arg	His	Phe	Ala	Gly	Asp	Val	Leu	Gly	Tyr	Val	Thr	Pro	Trp	Asn	Ser	
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	cat	ggc	tac	gat	gtc	acc	aag	gtc	ttt	ggg	agc	aag	ttc	aca	cag	atc	398
5	His	Gly	Tyr	Asp	Val	Thr	Lys	Val	Phe	Gly	Ser	Lys	Phe	Thr	Gln	Ile	
				95						100					105		
	tca	ccc	gtc	tgg	ctg	cag	ctg	aag	aga	cgt	ggc	cgt	gag	atg	ttt	gag	446
	Ser	Pro	Val	Trp	Leu	Gln	Leu	Lys	Arg	Arg	Gly	Arg	Glu	Met	Phe	Glu	
				110					115				120				
	gtc	acg	ggc	ctc	cac	gac	gtg	gac	caa	ggg	tgg	atg	cga	gct	gtc	agg	494
10	Val	Thr	Gly	Leu	His	Asp	Val	Asp	Gln	Gly	Trp	Met	Arg	Ala	Val	Arg	
				125					130				135				
	aag	cat	gcc	aag	ggc	ctg	cac	ata	gtg	cct	cgg	ctc	ctg	ttt	gag	gac	542
	Lys	His	Ala	Lys	Gly	Leu	His	Ile	Val	Pro	Arg	Leu	Lau	Phe	Glu	Asp	
				140				145				150					
15	tgg	act	tac	gat	gat	ttc	cgg	aac	gtc	tta	gac	agt	gag	gat	gag	ata	590
	Trp	Thr	Tyr	Asp	Asp	Phe	Arg	Asn	Val	Leu	Asp	Ser	Glu	Asp	Glu	Ile	
				155			160				165			170			
	gag	gag	ctg	agc	aag	acc	gtg	gtc	cag	gtg	gca	aag	aac	cag	cat	ttc	638
	Glu	Glu	Leu	Ser	Lys	Thr	Val	Val	Gln	Val	Ala	Lys	Asn	Gln	His	Phe	
20				175					180				185				
	gat	ggc	ttc	gtg	gtg	gag	gtc	tgg	aac	cag	ctg	cta	agc	cag	aag	cgc	686
	Asp	Gly	Phe	Val	Val	Glu	Val	Trp	Asn	Gln	Leu	Leu	Ser	Gln	Lys	Arg	
				190				195				200					
	gtg	ggc	ctc	atc	cac	atg	ctc	acc	cac	ttg	goc	gag	gct	ctg	cac	cag	734
25	Val	Gly	Leu	Ile	His	Met	Leu	Thr	His	Leu	Ala	Glu	Ala	Leu	His	Gln	
				205				210				215					
	gcc	cgg	ctg	ctg	gcc	ctc	ctg	gtc	atc	cgg	cct	goc	atc	acc	ccc	ggg	782
	Ala	Arg	Leu	Leu	Ala	Leu	Leu	Val	Ile	Pro	Pro	Ala	Ile	Thr	Pro	Gly	
				220			225				230						
30	acc	cag	cag	ctg	ggc	atg	ttc	acg	cac	aag	gag	ttt	gag	cag	ctg	goc	830
	Thr	Asp	Gln	Leu	Gly	Met	Phe	Thr	His	Lys	Glu	Phe	Glu	Gln	Leu	Ala	
				235			240				245			250			
	ccc	gtg	ctg	gat	ggt	ttc	agc	ctc	atg	acc	tac	gac	tac	tct	aca	gcg	878
	Pro	Val	Leu	Asp	Gly	Phe	Ser	Leu	Met	Thr	Tyr	Asp	Tyr	Ser	Thr	Ala	
35				255					260				265				

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926	cat cag cct ggc cct aat gca ccc ctg tcc tgg gtc cga gcc tgc gtc	280	270	275	280
	his gln pro gly pro asn ala pro leu ser trp val arg ala cys val				
974	cag gtc ctg gac ccg aag tcc aag tgg cga aga aat ctc ctg ggg	295	290	295	295
	gln val leu asp pro lys ser lys trp arg ser lys ile leu leu gly				
1022	ctc aac ttc tat ggt atg gac tac gcg acc tcc aag gat gcc cgt gag	305	300	305	310
	leu asn phe tyr gly met asp tyr ala thr ser lys asp ala arg gln				
1070	cct gtc gtc ggg gcc aag tac atc cag aca ctg aag gac cac aag ccc	320	315	325	330
	pro val val gly ala arg tyr ile gln thr leu lys asp his arg pro				
1118	cgg atg gtc tgg gac agc cag gcc tca gag cac ttc ttc gag tac aag	340	335	345	
	arg met val trp asp ser gln ala ser gln his phe gln tyr lys				
1166	aag agc cgc aat ggc aag gac gtc gtc ttc tac cca acc ctg aag tcc	360	355	365	
	lys ser arg ser gly arg his val val phe tyr pro thr leu lys ser				
1214	ctg cag gtc cgg ctg ggc cgg gac ctg ggc gtc ggc gtc tct	370	365	375	
	leu gln val arg leu gln leu ala arg gln leu gly val gly val ser				
1260	atc tgg aag ctg ggc cag ggc ctg gac tac ttc tac gac ctg ctc t	385	380	390	
	ile trp gln leu gly gln gly leu asp tyr phe tyr asp leu leu				
1320	aagtggtgcacat tgcggccctcc gcggtggacg tgcctctcttc taagccatgag agtgaagtgaag				
1357	caggtgtcgaa atacagacct caactccgct tgcctgctg				

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&lt;222&gt; (8)...(598)

&lt;221&gt; CDS

&lt;220&gt;

&lt;213&gt; Homo Sapiens

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&lt;212&gt; DNA

&lt;211&gt; 711

&lt;210&gt; 117

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	Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr
	15 20 25 30
	ctt gcc ctc ctg ggg ggc ccc acc tgg gca ggg aag atg tat ggc cct 145
	Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro
10	35 40 45
	gga gga ggc aag tat ttc agc acc act gaa gac tac gac cat gaa atc 193
	Gly Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile
	50 55 60
	aca ggg ctg cgg gtg tct gta ggt ctt ctc ctg gtg aaa agt gtc cag 241
15	Thr Gly Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln
	65 70 75
	gtg aaa ctt gga gac tcc tgg gac gtg aaa ctg gga gcc tta ggt ggg 289
	Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly
	80 85 90
20	aat acc cag gaa gtc acc ctg cag cca gcc gaa tac atc aca aaa gtc 337
	Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val
	95 100 105 110
	ttt gtc gcc ttc caa got ttc ctc cgg ggt atg gtc atg tac acc agc 385
	Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser
25	115 120 125
	aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct 433
	Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser
	130 135 140
	gcc tac ccc agc caa gag ggg cag gtg ctg gtg gcc atc tat ggc cag 481
30	Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln
	145 150 155
	tat caa ctc ctt gcc atc aag agc att gcc ttt gaa tgg aat tat cca 529
	Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro
	160 165 170
35	cta gag gag cgc acc act gag cca cca gtt aat ctc aca tac tca gca 577

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Leu Glu Glu Pro Thr Tyr Glu Pro Val Asn Leu Thr Tyr Ser Ala  
175 180 185  
aac tca ccc gtc gtc cgc tagggctgggg tatgggggcca tccggagctga ggcca  
630  
Asn Ser Pro Val Gly Arg  
195  
tctgtctgtgtgt ggttggtctgtat gttactctggag taaactagagtcg atctcgaatcc  
690  
accataaataat aagagcttctcg c  
711

5

10

<210> 118  
<211> 651  
<212> DNA  
<213> Homo Sapiens  
<220>  
<221> CDS  
<222> (242)...(565)

15

<400> 118  
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60  
ggcagagcgttc ggcacagggccg aaaggagcttc ggggggtctgggg gcttgggagtc cgtgtctcga  
120  
atcgaagggagg aagaaggtctggag tctgcgggggc tcaagggccggc cctcggagcatt gggcggagtgaa  
180  
gaagaaaggtcagg gaggcggagggc cttaaggttccct tccgggtctggag ggaagaaagggag ccaagcgaagga  
240  
g atg gag cag aag ctc gtc gag gag att ctt caa gaa atc act atg  
286  
Met Glu Glu Lys Leu Val Glu Glu Ile Leu Glu Ala Ile Thr Met  
15  
tca aca gac aca ggt gtc tcc ctc ctc tca tat gag gaa gat cag gaa  
334  
Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Glu Gly  
30  
tca aac ctc atc cga aaa gct aaa gag gca cca ttc gta ccc gtc gga  
382  
Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Gly  
40  
ata ggc ggt ttc gca gca atc gtc gca tat gga tca tat aaa ctc aag  
430  
Ile Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys  
50  
agc aag gag aat act aaa atg tcc atc cat ctc gac atc atc gtc  
478  
Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val

35

30

25

20



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	65	70	75	
	gca gcc caa ggc ttt gtt gta gga gca atg act gtt ggt atg ggc tat			526
	Ala Ala Gln Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr			
	80	85	90	95
5	tcc atg tat cgg gaa ttc tgg gca aaa cct aag cct tagaagaa			570
	Ser Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro			
	100	105		
	gagatgctgt cttggtcttg ttggaggagc ttgcttagt tagatgtctt attattaaag			630
	ttacctatta ttgttgaaa t			651
10	<210> 119			
	<211> 1310			
	<212> DNA			
	<213> Homo Sapience			
15	<220>			
	<221> CDS			
	<222> (78)...(1130)			
	<400> 119			
20	cgaagcgaag ggaggccacg tectgtctcc cctggtgaag aagctgcct gggtctgtcg			60
	tectagggtc tccagac atg tct gag gtg aag agc cgg aag aag tcg ggg			110
	Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly			
	1	5	10	
	ccc aag gga gcc cct gct gcg gag ccc ggg aag cgg agc gag ggc ggg			158
25	Pro Lys Gly Ala Pro Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Gly			
	15	20	25	
	aag acc ccc gtg gcc cgg agc agc gga ggc ggg ggc tgg gca gac ccc			206
	Lys Thr Pro Val Ala Arg Ser Ser Gly Gly Gly Trp Ala Asp Pro			
	30	35	40	
30	cga acg tgc ctg agc ctg ctg tcg ggg acg tgc ctg ggc ctg gcc			254
	Arg Thr Cys Leu Ser Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala			
	45	50	55	
	tgg ttt gta ttt cag cag tca gaa aaa ttt gca aag gtg gaa aac caa			302
	Trp Phe Val Phe Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln			
35	60	65	70	75

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350	tac	cag	tca	ctg	aaa	cta	gaa	acc	aat	gaa	tcc	caa	caa	ctc	caa	agt
398	tyr	gln	leu	leu	lys	leu	gln	thr	asn	gln	phe	gln	leu	gln	ser	
	aaa	atc	agt	tca	atc	tca	gaa	aag	tgg	cag	aaa	tct	gaa	gct	atc	atg
	90															
	85															
5	lys	ile	ser	leu	ile	ser	gln	lys	trp	gln	lys	ser	gln	ala	ile	met
	95															
	100															
446	gaa	caa	tgg	aag	tct	tct	caa	ata	att	gct	cat	cta	aag	cgt	cta	cag
	105															
	110															
10	gaa	gaa	atc	aat	gag	gta	aaa	act	tgg	tcc	aat	agg	ata	act	gaa	aaa
	120															
	115															
	110															
	gln	gln	leu	lys	ser	phe	gln	ile	ile	ala	his	leu	lys	arg	leu	gln
35	gag	aaa	gta	gaa	aaa	aat	aaa	aat	aaa	gta	aaa	aat	ata	ggt	gct	ctc
	125															
	130															
542	cag	gat	ata	ctg	aac	aac	agt	ctg	acg	acg	ctc	tct	caa	gac	atc	aca
	140															
	145															
590	aaa	gta	gac	caa	agt	aca	act	tcc	atg	gca	aaa	gat	glt	ggt	ctc	aag
	160															
	165															
638	att	aca	agt	gta	aaa	aca	gat	ata	cga	cgg	atc	tca	ggt	cta	gta	act
	170															
	180															
686	gat	gta	ata	tca	tgg	aca	gat	tct	gtg	caa	gaa	cta	gaa	aat	aaa	ata
	190															
	195															
734	gag	aaa	gta	gaa	aaa	aat	aca	gta	aaa	aat	ata	ggt	gac	ctc	ctc	tca
	200															
	205															
782	agc	agt	atc	gat	cga	aca	gca	acc	cga	aag	aca	gca	tct	gaa	aat	
	220															
	225															
830	tca	caa	aga	atc	aac	tct	gct	aag	aag	acc	cta	acc	gaa	cta	aag	agt
	230															
	235															
878	gac	tcc	gac	aaa	cat	aca	gtt	cta	agc	tta	gaa	ggt	gac	aga	aga	
	240															
	245															
	250															
85	asp	phe	asp	lys	his	thr	asp	arg	phe	leu	ser	leu	gln	gly	asp	arg

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	255	260	265	
	gcc aaa gtt ctg aag aca gtg act ttt gca aat gat cta aaa cca aag			926
	Ala Lys Val Leu Lys Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys			
	270	275	280	
5	gtg tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat			974
	Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn			
	285	290	295	
	gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta caa aga			1022
	Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg			
10	300	305	310	315
	gag aaa gaa att gct ttc tta agt gaa aaa ata tct aat tta aca ata			1070
	Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile			
	320	325	330	
	gtc caa gct gag att aag gat att aaa gat gaa ata gca cac att toa			1118
15	Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser			
	335	340	345	
	gat atg aat tagtttgaca ttattgagat tagactaagg taattttttt aat			1170
	Asp Met Asn			
	350			
20	gggacctctc atgagaagac tggtaaatca aaaataatga tttttggag caaaagtcac			1230
	tttatattta atctattttt gtacagtaaa aataaaactt taaaacaggt tgattttcca			1290
	aaataaatat gctaaaacct			1310
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25	<211> 1400			
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	<213> Homo Sapiens			
	<220>			
	<221> CDS			
30	<222> (233)...(556)			
	<400> 120			
	tggtctatgt ctattggagg gtggaaatca catctcctgt ttatccgtgt gcttgtagg			60
	tgtcagccgc caccocccoc ccatatgcag atttactcgg catggtatgt gccagcttct			120
35	aacacagctg gtatttcaag tctctggga cctcactcag gaatgatacc cctcagtag			180



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tttcccttgt tgacaattgc tctccagttc ctatgaaagc acagagcctt agggggcctg 1290
gccacagaaac acaaccatct taggcctgag ctgtgaacag caggggggttg tgtgtctgtt 1350
ctgtttctct gcttgccgaa cttttctaat aaacctatt tcttatttat 1400

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5  <210> 121
   <211> 483
   <212> PRT
   <213> Homo sapiens

10 <400> 121
Met Lys Ala Phe His Thr Phe Cys Val Val Leu Leu Val Phe Gly Ser
   1             5             10             15
Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile Val
   20             25             30
15 Glu Tyr Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp
   35             40             45
Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu
   50             55             60
Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly
20 65             70             75             80
Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro
   85             90             95
Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser
   100            105            110
25 Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His
   115            120            125
Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr
   130            135            140
Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn
30 145            150            155            160
Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu
   165            170            175
Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr
   180            185            190
35 Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp

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	195	205	200	205
	Cys Ser Gly Arg Val Cys Cys Gly Met Leu Ile Gly Leu Arg Phe			
	210	220	215	220
5	Leu Lys Arg Gln Asp Leu Lys Val Leu Ala Arg Met Met Arg Pro	225	230	235
	240			
	Val Ser Asp Gln Val Ile Lys Val Thr Met Asn Asp Gln Asp Met	245	250	255
	Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Leu	260	265	270
10	Gln Lys Gln Met Gln Asp Leu Ser Gln Phe Cys Ser Asp Lys Pro Lys	275	280	285
	Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser Gln	290	295	300
	Met Gly Gln Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe	305	310	315
15	Leu Thr His Tyr Ala Asp Lys Ile Gln Ser Val His Phe Ser Asp Gln	320		330
	325	330		335
	Phe Ser Gly Pro Lys Ile Met Gln Gln Gly Gln Pro Leu Lys Leu	340	345	350
20	Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser	355	360	365
	Gly Asn Thr Tyr Pro Lys Asp Met Gln Ala Leu Leu Pro Leu Met Asn	370	375	380
	Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Phe Arg Leu Asn Arg	385	390	395
25	Gln Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Gln Gln Asn	400		410
	405	410	415	
	Phe Leu Lys Leu Thr His Val Gln Arg Gln Gln Ala Ala Gln Ser Arg	420	425	430
30	Arg Gln Gly Lys Arg Ala Gln Lys Gln Arg Ile Met Asn Gln Gln	435	440	445
	Asp Pro Gln Lys Gln Arg Arg Leu Gln Ala Ala Leu Arg Arg Gln	450	455	460
35	Gln Lys Leu Gln Lys Met Lys Met Lys Gln Ile Lys Val	465	470	475
	480			

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Lys Ala Met

&lt;210&gt; 122

&lt;211&gt; 334

5 &lt;212&gt; PRT

&lt;213&gt; Homo sapience

&lt;400&gt; 122

Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg Arg Leu Gln  
 10           1                   5                   10                   15  
 Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu  
                  20                   25                   30  
 Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu  
                  35                   40                   45  
 15 Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro  
          50                   55                   60  
 Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp  
          65                   70                   75                   80  
 Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu  
 20                   85                   90                   95  
 Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val  
                  100                   105                   110  
 Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe  
                  115                   120                   125  
 25 Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu  
          130                   135                   140  
 Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu  
          145                   150                   155                   160  
 Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly  
 30                   165                   170                   175  
 Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu  
                  180                   185                   190  
 Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn Arg Lys Gly  
          195                   200                   205  
 35 Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe

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	210	215	220
	Set phe Gly Gln Asn Asp Leu phe Asp Gln Ile Pro Asn Ser Ser Gly		
	225	230	235
	Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile		
5	245	250	255
	Ser Leu Pro Leu phe His Gly Arg Gly Val phe Gln Tyr Ser phe Gly		
	260	265	270
	Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile		
	275	280	285
	Gln Val Gln Lys Thr Leu His Pro Ser Gln Gln Val Asn Gln Leu		
10	290	295	300
	His Gln Arg Tyr Ile Lys Gln Leu Cys Asn Leu phe Gln Ala His Lys		
	305	310	315
	Leu Lys phe Asn Ile Pro Ala Asp Gln His Leu Gln phe Cys		
15	325	330	
	<210> 123		
	Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly		
	1	5	10
	His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu phe Leu His Asp		
	20	25	30
	Thr Gln Leu Arg Gln Trp Gln Gln Gly Gln Leu Leu Pro Leu		
	35	40	45
	Thr phe Leu Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val		
30	50	55	60
	Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln		
	65	70	75
	Gln Leu Lys Gln Gln Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu		
	85	90	95
	Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His		
35			



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100 105 110  
 Cys Arg Glu Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro  
 115 120 125  
 Trp Met Glu Asn Cys Val Gly Glu Arg Asn His Pro Leu Phe Val Val  
 5 130 135 140  
 Tyr Leu Ala Leu Gln Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala  
 145 150 155 160  
 Trp Ser Gly Leu Arg Phe Phe Gln Pro Trp Gly Leu Trp Leu Arg Ser  
 165 170 175  
 10 Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Leu Ser Leu Phe Ser Leu  
 180 185 190  
 Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn  
 195 200 205  
 Thr Thr Thr Trp Glu Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg  
 15 210 215 220  
 Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala  
 225 230 235 240  
 His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Glu Thr Leu Trp Ala  
 245 250 255  
 20 Glu Glu Glu Glu Glu Gly Ser Ser Pro Ala Val  
 260 265  
  
 <210> 124  
 <211> 106  
 25 <212> PRT  
 <213> Homo sapience  
  
 <400> 124  
 Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu  
 30 1 5 10 15  
 Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala Leu Asp Asp Pro  
 20 25 30  
 Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly  
 35 40 45  
 35 Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser

[illegible]

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165 170 175  
 Val Tyr Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu  
 180 185 190  
 Gly Ser Trp Ala Ala Leu Leu Ala Arg Ala Val Thr Gly Leu Leu  
 5 195 200 205  
 Ala Leu Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser  
 210 215 220  
  
 <210> 126  
 10 <211> 258  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 126  
 15 Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val Tyr Ser Val Pro Arg  
 1 5 10 15  
 Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu Leu Ser Ala Leu Leu  
 20 25 30  
 Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro Pro Leu Cys His Gly  
 20 35 40 45  
 Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys Asp Phe Asp Trp Arg  
 50 55 60  
 Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile Val Met Met Lys Asn  
 65 70 75 80  
 25 Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly  
 85 90 95  
 Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu  
 100 105 110  
 Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp  
 30 115 120 125  
 Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu  
 130 135 140  
 Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg  
 145 150 155 160  
 35 Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr

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165 170 175

Lys Gln Leu Pro Thr Leu Ile Leu Phe Gln Gly Lys Gln Ala Met  
180 185 190Arg Arg Pro Gln Ile Asp Lys Lys Gly Arg Ala Val Ser Thr Phe  
195 200 205Ser Gln Gln Asn Val Ile Arg Gln Phe Asn Leu Asn Gln Leu Tyr Gln  
210 215 220Arg Ala Lys Lys Leu Ser Lys Ala Gly Asp Asn Ile Pro Gln Gln Gln  
225 230 235 240Pro Val Ala Ser Thr Pro Thr Thr Val Ser Asp Gly Gln Asn Lys Lys  
245 250 255

Asp Lys

&lt;210&gt; 127

&lt;211&gt; 110

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 127

Met Ala Ala Val Val Ala Lys Arg Gln Gly Pro Pro Phe Ile Ser Gln  
1 5 10 15Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser  
20 25 30Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly  
35 40 45Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Leu Ser Leu  
50 55 60Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn Lys Tyr Phe Lys Ser  
65 70 75 80Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly Gly Leu Phe Thr Tyr  
85 90 95Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr  
100 105 110

35 &lt;210&gt; 128

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&lt;211&gt; 91

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

5 &lt;400&gt; 128

Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser

1 5 10 15

Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu

20 25 30

10 Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys

35 40 45

Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp Gly Arg

50 55 60

Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu

15 65 70 75 80

Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly

85 90

&lt;210&gt; 129

20 &lt;211&gt; 344

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 129

25 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser

1 5 10 15

Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu

20 25 30

Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val

30 35 40 45

Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys

50 55 60

Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe

65 70 75 80

35 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu

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5	85	90	95	Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Gln Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser 130 135 140 Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr 145 150 155 Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly 165 170 175 Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys 180 185 190 Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser 195 200 205 Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Gln Pro Ile Phe Ser Ser 210 215 220 Ser Gln Pro Thr Ser Gln Ala Arg Ile Gly Met Gly Ala Thr Leu Asp 225 230 235 Ile Gln Arg Gln Gln Arg Met Gln Leu Asp Arg Gln Leu Met Phe 245 250 255 Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Met 260 265 270 Ile Asn Trp Asn Arg Leu Phe Pro Leu Arg Gln Arg Gln Asn Val 275 280 285 Asn Tyr Gln Gly Arg Gln Ser Gln Pro Ala Ala Pro Leu Gln 290 295 300 Val Ser Gln Gln Val Ala Arg Leu Met Gln Met Gly Phe Ser Arg 305 310 315 Gly Asp Ala Leu Gln Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val 325 330 335 Ala Thr Asn Phe Leu Gln His
35	<210> 130			

149/177

&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

5 &lt;400&gt; 130

Met Gly Pro Pro Pro Gly Ala Gly Val Ser Cys Arg Gly Gly Cys Gly

1 5 10 15

Phe Ser Arg Leu Leu Ala Trp Cys Phe Leu Leu Ala Leu Ser Pro Gln

20 25 30

10 Ala Pro Gly Ser Arg Gly Ala Glu Ala Val Trp Thr Ala Tyr Leu Asn

35 40 45

Val Ser Trp Arg Val Pro His Thr Gly Val Asn Arg Thr Val Trp Glu

50 55 60

Leu Ser Glu Glu Gly Val Tyr Gly Gln Asp Ser Pro Leu Glu Pro Val

15 65 70 75 80

Ala Gly Val Leu Val Pro Pro Asp Gly Pro Gly Ala Leu Asn Ala Cys

85 90 95

Asn Pro His Thr Asn Phe Thr Val Pro Thr Val Trp Gly Ser Thr Val

100 105 110

20 Gln Val Ser Trp Leu Ala Leu Ile Gln Arg Gly Gly Cys Thr Phe

115 120 125

Ala Asp Lys Ile His Leu Ala Tyr Glu Arg Gly Ala Ser Gly Ala Val

130 135 140

Ile Phe Asn Phe Pro Gly Thr Arg Asn Glu Val Ile Pro Met Ser His

25 145 150 155 160

Pro Gly Ala Val Asp Ile Val Ala Ile Met Ile Gly Asn Leu Lys Gly

165 170 175

Thr Lys Ile Leu Gln Ser Ile Gln Arg Gly Ile Gln Val Thr Met Val

180 185 190

30 Ile Glu Val Gly Lys Lys His Gly Pro Trp Val Asn His Tyr Ser Ile

195 200 205

Phe Phe Val Ser Val Ser Phe Phe Ile Ile Thr Ala Ala Thr Val Gly

210 215 220

Tyr Phe Ile Phe Tyr Ser Ala Arg Arg Leu Arg Asn Ala Arg Ala Gln

35 225 230 235 240

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35	atcnaagacc ctcgaactc ctgctgtctc cttctgtgtc ttggtaggt ctcgaagc	60
	agattctgaag atctcactgtc actcnaagcc ctcnaaggt cctactcact	180
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	Val Gln Gly Thr Asp Gln Pro Leu Gln Gln His Val Gln Ser Thr	365
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15	His Gln Asp Asn Arg Ser Gln Thr Ala Ser Ser Gly Tyr Ala Ser	350
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	Ile Leu Lys Ala Leu Gly Ile Gln Val Asp Val Gln Asp Gly Ser Val	320
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	Leu Val Arg Ile Leu Thr Cys Asn His Ile Phe His Lys Thr Cys Val	285
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5	Asp Gly Asp Ser Cys Ala Val Cys Ile Gln Ileu Tyr Lys Pro Asn Asp	270
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	245	
	250	
	Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Ala Ile Gly	



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	cggaaactaca ttgcgggctt ccaccccoat ggagtctctg cagtcggagc ctttgccaac	360
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[illegible][illegible]

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&lt;400&gt; 134

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 ggcgatgatc tcagcatgtg cggcctcatg cttaaagtga agtgggtgtg ttgggtcgtc 180  
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10

&lt;210&gt; 135

&lt;211&gt; 672

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

15

&lt;400&gt; 135

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 accactctct ttgtccaaat ctgcaagatg ctgttcttgg ccactttctt tccacactgg 180  
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35

&lt;400&gt; 136

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10	atcggtcccgccg tgggtctgagggg ccgctcgtccaca gcccgcgtcccg ccgctcgtcccg ggcgcgtcccg ccgctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg ccgctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg ccgctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg tccctcgtcccg	60 120 180 240 300 330
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	Ser	Val	Ser	Glu	Ala	Lys	Phe	Asp	Asp	Phe	Glu	Asp	Glu	Glu	Asp	Ile	
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	gta	gag	tat	gat	gat	aat	gac	ttc	gct	gaa	ttt	gag	gat	gtc	atg	gaa	262
	Val	Glu	Tyr	Asp	Asp	Asn	Asp	Phe	Ala	Glu	Phe	Glu	Asp	Val	Met	Glu	
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	gac	tct	gtt	act	gaa	tct	cct	caa	cgg	gtc	ata	atc	act	gaa	gat	gat	310
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	gaa	gat	gag	acc	act	gtg	gag	ttg	gaa	ggg	cag	gat	gaa	aac	caa	gaa	358
	Glu	Asp	Glu	Thr	Thr	Val	Glu	Leu	Glu	Gly	Gln	Asp	Glu	Asn	Gln	Glu	
						65					70				75		
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	Gly	Asp	Phe	Glu	Asp	Ala	Asp	Thr	Gln	Glu	Gly	Asp	Thr	Glu	Ser	Glu	
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	cca	tat	gat	gat	gaa	gaa	ttt	gaa	ggt	tat	gaa	gac	aaa	cca	gat	act	454
	Pro	Tyr	Asp	Asp	Glu	Glu	Phe	Glu	Gly	Tyr	Glu	Asp	Lys	Pro	Asp	Thr	
20						100					105				110		
	tct	tct	agc	aaa	aat	aaa	gac	cca	ata	acg	att	gtt	gat	gtt	cct	gca	502
	Ser	Ser	Ser	Lys	Asn	Lys	Asp	Pro	Ile	Thr	Ile	Val	Asp	Val	Pro	Ala	
						115					120				125		
	cac	etc	cag	aac	agc	tgg	gag	agt	tat	tat	cta	gaa	att	ttg	atg	gtg	550
25	His	Leu	Gln	Asn	Ser	Trp	Glu	Ser	Tyr	Tyr	Leu	Glu	Ile	Leu	Met	Val	
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	act	ggt	ctg	ctt	gct	tat	atc	atg	aat	tac	atc	att	ggg	aag	aat	aaa	598
	Thr	Gly	Leu	Leu	Ala	Tyr	Ile	Met	Asn	Tyr	Ile	Ile	Gly	Lys	Asn	Lys	
						145					150				155		
30	aac	agt	cgc	ctt	gca	cag	gcc	tgg	ttt	aac	act	cat	agg	gag	ctt	ttg	646
	Asn	Ser	Arg	Leu	Ala	Gln	Ala	Trp	Phe	Asn	Thr	His	Arg	Glu	Leu	Leu	
						160					165				170		
	gag	agc	aac	ttt	act	tta	gtg	ggg	gat	gat	gga	act	aac	aaa	gaa	gcc	694
	Glu	Ser	Asn	Phe	Thr	Leu	Val	Gly	Asp	Asp	Gly	Thr	Asn	Lys	Glu	Ala	
35						180					185				190		

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742	aca agc aca gga aag tgc aac cag gag aat gag cac atc tac aac ctg Ther Ser Thr Gly Lys Leu Asn Gln Gln Asn Gln Hls Ile Tyr Asn Leu	195 200 205
790	tgg tgt tct ggt cga gtc tgc tgc gag ggc atg ctt atc cag ctg aag Trp Cys Ser Gly Arg Val Cys Cys Gln Gly Met Leu Ile Gln Leu Arg	210 215 220
838	tcc ctg aag aga caa gac tca ctg aat gtc ctg gcc cgg atg atg aag Phe Leu Lys Arg Gln Asp Leu Asn Val Leu Ala Arg Met Met Arg	225 230 235
886	cca gtc agt gat cca gtc caa ata aaa gta acc atg aat gat gaa gac Pro Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Gln Asp	240 245 250 255
934	atg gat acc tac gta ttt gct gtc ggc aca cgg aaa gcc tgc gtc cga Met Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg	260 265 270
982	cta cag aaa gag atg cag gat tgc agt gag ttc tgt agt gat aac cct Leu Gln Lys Gln Met Gln Asp Leu Ser Gln Phe Cys Ser Asp Lys Pro	280 285
1030	aag tcc gga aag tat gga ctg ccg gac tcc tgc gcc atc ctg tca Lys Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Ser Leu Ala Ile Leu Ser	290 295 300
1078	gag atg gga gaa gtc aca gac gga atg atg gat aca aag atg gtc cac Gln Met Gly Gln Val Thr Asp Gly Met Met Asp Thr Lys Met Val His	310 315
1126	ttt ctt aca cac tat gct gag aag atc gaa tcc gtt cat ttt tca gac Phe Leu Thr His Tyr Ala Asp Lys Ile Gln Ser Val His Phe Ser Asp	320 325 330 335
1174	cag ttc tcc ggt cca aaa atc atg caa gag gaa ggt cag cct tta aag Gln Phe Ser Gly Pro Lys Ile Met Gln Gln Gln Gly Gln Pro Leu Lys	340 345 350
1222	cta cct gac act aag aag aca ctg tgc ttc aca ttt aat gtc cct ggc Leu Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly	355 360 365
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	Asn Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn			
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5	aga gaa ggc aaa caa aaa gca gat aag aac cgt gcc cga gta gaa gag			1366
	Arg Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu			
	400	405	410	415
	aac ttc ttg aaa ctg aca cat gtg caa aga cag gaa gca gca cag tot			1414
	Asn Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser			
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	cgg cgg gag gag aaa aaa aga gca gag aag gag cga atc atg aat gag			1462
	Arg Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu			
	435	440	445	
	gaa gat cct gag aaa cag cgc agg ctg gag gag gct gca ttg agg cgt			1510
15	Glu Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg			
	450	455	460	
	gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa caa atc aaa			1558
	Glu Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys			
	465	470	475	
20	gtg aaa gcc atg taaagccatc ccagagattt gagttctgat gccacctgta			1610
	Val Lys Ala Met			
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156			

phe trp leu leu thr val leu tyr ala ala trp trp tyr leu asp arg  
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 gac aag cca cgg cag ggg ggc cgc cag cac atc cag gcc atc agg tgc tgg  
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25	act gct gag cty gac ccc tct cgy aac tac att gcg ggc ttc cac ccc	80	85	90	396
					The Ala Glu Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro

492 aua ggc ttc tct lcg atc ttc ccc ggt atc cgc acc cat ctg atg  
 130 The Gly phe ser Ile phe pro Gly Ile Arg pro His Leu Met  
 135  
 140

540 cga acc tga tga ttc cgg gcc ccc ttc ttc aga gat tac atc atg tct  
35 leu thr leu trp phe arg ala pro phe phe arg asp tyr ile met ser

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	160	165	170	
5	agg aag ggt ggc gga aac ttg ctg ggc atc att gta ggg ggt gcc cag			636
	Arg Lys Gly Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln			
	175	180	185	
	gag gcc ctg gat gcc agg cct gga tcc ttc acg ctg tta ctg cgg aac			684
	Glu Ala Leu Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn			
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	cga aag ggc ttc gtc agg ctc gcc ctg aca cac ggg gca ccc ctg gtg			732
	Arg Lys Gly Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val			
	210	215	220	
	cca atc ttc tcc ttc ggg gag aat gac cta ttt gac cag att ccc aac			780
15	Pro Ile Phe Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn			
	225	230	235	
	tct tct ggc tcc tgg tta cgc tat atc cag aat cgg ttg cag aag atc			828
	Ser Ser Gly Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile			
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	Met Gly Ile Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr			
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	agc ttt ggt tta ata ccc tac cgc cgg ccc atc acc act gtg gtg ggg			924
	Ser Phe Gly Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly			
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	aag ccc atc gag gta cag aag acg ctg cat ccc tcg gag gag gag gtg			972
	Lys Pro Ile Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val			
	290	295	300	
	aac cag ctg cac cag cgt tat atc aaa gag ctg tgc aac ctc ttc gag			1020
30	Asn Gln Leu His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu			
	305	310	315	
	gcc cac aaa ctt aag ttc aac atc cct gct gac cag cac ttg gag ttc			1068
	Ala His Lys Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe			
	320	325	330	
35	tgc tgagcccaa agggcagggc caacattagg gagccagca ggaggtgctg			1120

[illegible]

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&lt;221&gt; CDS

&lt;222&gt; (32)...(835)

&lt;400&gt; 143

5	attttcttcggtgtggggccccgggcccaggagc g atg gcg ccc tgg gcg etc etc	52
	Met Ala Pro Trp Ala Leu Leu	
	1 5	
	agc cct ggg gtc ctg gtg cgg acc ggg cac acc gtg ctg acc tgg gga	100
	Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly	
10	10 15 20	
	atc acg ctg gtg etc ttc ctg cac gat acc gag ctg cgg caa tgg gag	148
	Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Gln Trp Glu	
	25 30 35	
	gag cag ggg gag ctg etc ctg ccc etc acc ttc ctg etc ctg gtg ctg	196
15	Glu Gln Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Leu Val Leu	
	40 45 50 55	
	ggc tcc ctg ctg etc tac etc gct gtg tca etc atg gac cct ggc tac	244
	Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr	
	60 65 70	
20	gtg aat gtg cag ccc cag cct cag gag gag etc aaa gag gag cag aca	292
	Val Asn Val Gln Pro Gln Pro Gln Glu Glu Leu Lys Glu Glu Gln Thr	
	75 80 85	
	gcc atg gtt cct cca gcc atc cct ctt cgg cgc tgc aga tac tgc ctg	340
	Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu	
25	90 95 100	
	gtg ctg cag ccc ctg agg gct cgg cac tgc cgt gag tgc cgc cgt tgc	388
	Val Leu Gln Pro Leu Arg Ala Arg His Cys Arg Glu Cys Arg Arg Cys	
	105 110 115	
	gtc cgc cgc tac gac cac cac tgc ccc tgg atg gag aac tgt gtg gga	436
30	Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly	
	120 125 130 135	
	gag cgc aac cac cca etc ttt gtg gtc tac ctg gcg ctg cag ctg gtg	484
	Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Gln Leu Val	
	140 145 150	
35	gtg ctt ctg tgg ggc ctg tac ctg gca tgg tca ggc etc cgg ttc ttc	532

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35	<221> CDS	
	<220>	
	<213> Homo sapiens	
	<212> DNA	
30	<211> 619	
	<210> 144	
25	aatctaatatata aaggaagttcc agtcctc aagcagaagaccac ggggtctccacc ccaagcccccgc ccaaggtctgctt gcccagtgccac accttttcaaca ggcagaagttctctg cctctccaaagg aagaaaggggga agaaagaaagaaac ctggtgtgggtgg ctcacagggccaa tgcaccaccagcc tcccaagagacc cagaaagggaag cttccaaagttca gaaagaaatctcc tgcctctgtgtg aaaccaccaggg gtcctgtccccc agctctgggtgt agcgtctcaga gggcctgggg cctccaccatcc	930 990 1050 1110 1136
20	265 Ser Pro Ala Val aga cca gct gtc taggttctgct ggaagcccggg ctaccgtctct gtgcctga	870
15	250 Ser Gly Ser Trp Glu Thr Leu Trp Ala Glu Glu Glu Gly Ser tca ggg tcc tgg gag acc ctc tgg gct gag gaa gag gaa gaa ggc agc asp arg gly leu thr arg asn leu ala his phe phe cys gly trp pro	820
10	235 240 245 gac cga ggc ctg acc cgc acc ctc ggc cac ttc tgc gga tgg ccc asp arg gly leu thr arg asn leu ala his phe phe cys gly trp pro Ser Ser His Arg Ile Ala Tyr Leu Arg Glu Arg Pro Ser Asn Pro Phe tcc tca cac cgc atc gcc tat ctc cgc cag cgc acc agc acc ccc ttc Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Trp Glu Phe Ile	772 724
5	200 205 210 215 230 225 220 tcc gac ctc tac ctg gtc agc acc acc acc acc tgg gaa ttc atc phe leu leu leu leu phe ser leu phe ser leu ala ser leu leu leu val tcc ctg ctg ctg tcc ctc tcc tcc tcc tcc tcc gtc ggc agc agc ctg ctc atc Gln Pro Trp Gly Leu Trp Leu Arg Ser Ser Gly Leu Leu Phe Ala Thr cag ccc tgg ggt ctc agc tgg tgg tgg cgg tcc agc ggg ctc ctg gcc acc Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe	676 628 580

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$\langle 222 \rangle \quad (13) \dots (333)$

<400> 144

	cttcgactgc ct atg tcc act aac aat atg tcg gac cca cgg agg cgg	48
5	Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro	
	1 5 10	
	aac aaa gtg ctg agg tac aag ccc ccg cgg agc gaa tgt aac cgg gcc	96
	Asn Lys Val Leu Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala	
	15 20 25	
10	ttg gac gac cgg acg cgg gac tac atg aac ctg ctg ggc atg atc ttc	144
	Leu Asp Asp Pro Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe	
	30 35 40	
	agc atg tgc ggc ctc atg ctt aag ctg aag tgg tgt got tgg gtc got	192
	Ser Met Cys Gly Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala	
15	45 50 55 60	
	gtc tac tgc tcc ttc atc agc ttt gcc aac tct cgg agc tcg gag gac	240
	Val Tyr Cys Ser Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp	
	65 70 75	
	acg aag caa atg atg agt agc ttc atg ctg tcc atc tct gcc gtg gtg	288
20	Thr Lys Gln Met Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val	
	80 85 90	
	atg tcc tat ctg cag aat cct cag ccc atg acg ccc cca tgg	340
	Met Ser Tyr Leu Gln Asn Pro Gln Pro Met Thr Pro Pro Trp	
	95 100 105	
25	tgataccagc ctagaagggc cacaatttgg accctgtcta tccactagga ctggggtttg	390
	gctgctaaac ctgctgcttt cagctgccat cctggacttc cctgaatgag gcgctctcgg	450
	tgccccacgc tggatagagg gaacctggcc ctttctcagg gaacacccta ggcttaaccc	510
	tactgcctcc ctcccccctg ctgctgctgg gggagatgct gtccatgttt ctagggggat	570
	tcatttgctt tctcgttgaa acctgttgtt aataaagttt ttcaactcag	619
30		
	<210> 145	
	<211> 864	
	<212> DNA	
	<213> Homo sapience	
35	<220>	





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atc gtc gcg tct gct cag gtc tgg atg ata aca cgc tat gat ctg tac 596  
 Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr  
 150 155 160  
 cac acc ttc cgg cca gct gtc ctc ctg atg ttc ctc agt gtc tac 644  
 5 His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr  
 165 170 175  
 aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc tgc ctg gcc agt 692  
 Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser  
 180 185 190  
 10 tgg gca gct cta ctg gcc cga gca gtc gta acg ggg ctg ctg gcc ctc 740  
 Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu  
 195 200 205 210  
 agc act ttg gcc ctg tat gtc gcc gtt gtc aat gtg cac tcc taggcttg 790  
 Ser Thr Leu Ala Leu Tyr Val Ala Val Asn Val His Ser  
 15 215 220  
 gtgtctcaga cattgatgta ccttttccct gctcgtctcc aggttttagt gaagtaaaca 850  
 gtatttgga agtt 864  
  
 <210> 146  
 20 <211> 1527  
 <212> DNA  
 <213> Homo sapience  
 <220>  
 <221> CDS  
 25 <222> (25)...(801)  
  
 <400> 146  
 gcagtgccg ttaaggccga aaag atg gcg gtc ttg gca cct cta att gct 51  
 Met Ala Val Leu Ala Pro Leu Ile Ala  
 1 5  
 30 ctc gtg tat tgc gtg cgg cga ctt tca cga tgg ctc gcc caa cct tac 99  
 Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr  
 10 15 20 25  
 tac ctt ctg tgc gcc ctg ctc tct gct gcc ttc cta ctc gtg agg aaa 147  
 35 Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

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195	ctg cgg cgg ctc tgc cac ggt ctg ccc acc cca cgc gaa gac ggt aac	30	40
195	leu pro pro leu cys his gly leu pro thr gln arg gln asp gly asn	35	40
243	ccg tgt gac ttc gac tgc aga gaa gtc gag atc ctg atg ttc ctg agt	45	50
243	pro cys asp phe asp thr arg gln val gln ile leu met phe leu ser	55	60
291	gcc att gtc atg atg aac cgc aga tcc atg ttc ctg atg acc tgc	65	70
291	ala ile val met met lys asn arg ser met phe leu met thr cys	75	80
339	aaa ccc ccc cta tat atg ggc cct gag tat atc aag tac ttc atg gat	85	
339	lys pro pro leu tyr met gly pro gln tyr ile lys tyr phe asn asp	90	100
387	aaa acc att gat gag gaa cta gaa cgg gac aag agg gtc act tgg atc	105	
387	lys thr ile asp gln leu leu arg asp lys arg val thr trp ile	110	120
435	gtc gag ttc ttc gcc atc tgg tct atg gac tgc cca tca ttc gcc cct	115	120
435	val gln phe phe ala asn trp ser asn asp cys gln ser phe ala pro	130	135
483	atc tat gtc gac ctc tcc acc tga aac tgc aca ggg cta atc ttc	140	145
483	ile tyr ala asp leu ser leu lys tyr asn cys thr gly leu asn phe	150	
531	ggg aag gtc gat gtc gga cgc tat act gat gtc agt acc cgg tac aaa	155	160
531	gly lys val asp val gly arg tyr thr asp val ser thr arg tyr lys	165	
579	gtg agc aca tca ccc ctc acc aag caa ctc cct acc ctg atc ctg ttc	170	180
579	val ser thr ser pro leu thr lys gln leu pro thr leu ile leu phe	185	
627	cna gtc ggc aag gag gaa atg cgg cgg cca cag atc gac aag aca gga	190	200
627	gln gly gly lys gln ala met arg arg pro gln ile asp lys gly	205	
675	cgg gtc gtc tca tgg acc ttc tct gag gag nat gtc atc cga gaa ttc	210	215
675	arg ala val ser trp thr phe ser gln gln asn val ile arg gln phe	220	
723	aat tta aat gag cta tac cag cgg gcc aag aca cta tca aag gct gga	225	

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Asn Leu Asn Glu Leu Tyr Gln Arg Ala Lys Lys Leu Ser Lys Ala Gly
      220              225              230
gac aat atc cct gag gag cag cct gtg gct tca acc ccc acc aca gtg      771
Asp Asn Ile Pro Glu Glu Gln Pro Val Ala Ser Thr Pro Thr Thr Val
5      235              240              245
tca gat ggg gaa aac aag aag gat aaa taagatcctc ac      810
Ser Asp Gly Glu Asn Lys Lys Asp Lys
      250              255
tttggcagtg cttcctctcc tgtcaattcc aggcctcttc cataaccaca agcctgaggc      870
10 tgcagccttt tatttatgtt ttccctttgg ctgtgactgg gtggggcagc atgcagcttc      930
tgattttaaa gaggcattcta gggaattgtc aggcacccta caggaaggcc tgcctagtgt      990
tggccaaactg ttctactgga gcaagaaaga gatctcatag gacggagggg gaaatggttt      1050
ccctccaagc ttgggtcagt gtgttaactg cttatcagct attcagacat ctccatggtt      1110
tctccatgaa actctgtggt ttcacatcct cttcttagtt gacctgcaca gcttggttag      1170
15 acctagattt aaccctaagg taagatgctg gggtatagaa cgctaagaat ttcccccaa      1230
ggactcttgc ttccctaagc ccttctggct tcgtttatgg tcttcattaa aagtataagc      1290
ctaaotttgt cgctagtctc aaggagaaac ctttaaccac aaagttttta tcattgaaga      1350
caatattgaa caaccoccta ttttgtggg attgagaagg ggtgaataga ggccttgagac      1410
tttcccttgt gtggtaggac ttggaggaga aatccccggt actttcacta accctctgac      1470
20 atactcecca cccccagttg atggctttcc gtaataaaaa gattgggatt tcccttt      1527

<210> 147
<211> 659
<212> DNA
25 <213> Homo sapiens
<220>
<221> CDS
<222> (138)...(470)

30 <400> 147
agtcttcoga gcaagatggc gccgcgggca tttcttcaca tgcctgtctg agggaaacgt      60
aagtagtggt tcgcggcgcg tgtccagct ccgcgttgtt ccgcgagaaa gcgagaggcc      120
gagcccgggc tggtgcg atg gcc gcg gtg gtg gcc aag cgg gaa ggg cgg      170
Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro
35      1              5              10

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218

266 tat tgc cgg acc tgc gtc tca gcc ctg tgc ggg gcc acc gcc atc  
Tyr Cys Arg Thr Ser Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile

45	50	55
Leu Gly Leu Thr Gly Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser		

60	65	70	75	410
----	----	----	----	-----

458 ggc ctc ttc acc tac gtc ctg ttc tgg acc ttc ctc tac ggc atg gtc

THE VALLEY

659 **ՀԱՅԿԱՅԻՆ ԴԱՏԱՎԱՐՈՒԹՅԱՆ ԿԱԶՄԱՆԻԿԱՆ ԿԵՆՏՐԱԼԻԶԱԿԱՆ ԿՈՄԻՏԵ**

<212> DNA

... <2222> (68)... (343)

၀၉      ဂ်ဒဲးဗုဒ္ဓဂ်ဂ်ဂ်ဂ် ဂ်ဗုဒ္ဓဂ်ဂ်ဂ်ဂ် ဂ်ဂ်ဂ်ဂ်ဂ်ဂ် ဂ်ဂ်ဂ်ဂ်ဂ်ဂ် ဂ်ဂ်ဂ်ဂ်ဂ်ဂ် ဂ်ဂ်ဂ်ဂ်ဂ်ဂ်

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	ggacaag atg gtt tac atc tgc aac gga caa gtg ttg gac agc cgg agt	109
	Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser	
	1 5 10	
	cag tct cca tgg aga tta tct ttg ata aca gat ttc ttc tgg gga ata	157
5	Gln Ser Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile	
	15 20 25 30	
	gct gag ttt gtg gtt ttg ttt ttc aaa act ctg ctt cag caa gat gtg	205
	Ala Glu Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val	
	35 40 45	
10	aaa aaa aga aga agc tat gga aac tca tot gat tcc aga tat gat gat	253
	Lys Lys Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp	
	50 55 60	
	gga aga ggg cca cca gga aac cct ccc cga aga atg ggt aga atc aat	301
	Gly Arg Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn	
15	65 70 75	
	cat ctg cgt ggc cct agt ccc cct cca atg gct ggt gga tgaggaaggt	350
	His Leu Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly	
	80 85 90	
	aaatgtctgc tctaagaagc agacaaccgg acatgcgcac tcatagcaga aggaaccat	410
20	caagaagtgg aaggtcgacc atgatgagca gtagatgaat gtgtatgtct aaacaaggac	470
	tgtctctgtg cctcacagat gaatgaggtc atgctgggaa ttcctctgc agggaaactgg	530
	cctgactgac atgcagttcc ataatgcag atgtttgtct cattaccttt ttgtatagtt	590
	tattaaagta ttaatatagt tttaataagt aaatattttt aggttgcaga atggactcct	650
	catctttata ttcacgaaaa agcaatctga agaaaacaaa taaaagcctg tgtatttagc	710
25		
	<210> 149	
	<211> 2182	
	<212> DNA	
	<213> Homo sapience	
30	<220>	
	<221> CDS	
	<222> (56)...(1090)	
	<400> 149	
35	gcacttcagc ttcacctccc caggcgccct ctggggctcc gagccggcg ggacc	58

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103	Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser 1 5 10 15	atg ttc acc agc acc ggc tcc agt ggg ctc tac aag ggc cct ctg tcc Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser 1 5 10 15
151	aag agc ctc ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc ggc ctc Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu 20 25 30	aag agc ctc ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc ggc ctc Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu 20 25 30
199	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctc cac gca gtc Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val 35 40 45	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctc cac gca gtc Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val 35 40 45
247	aag aac gac ttc cag att tgy agg ttg ata tgt gga aga ata att tgc Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys 50 55 60	aag aac gac ttc cag att tgy agg ttg ata tgt gga aga ata att tgc Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys 50 55 60
295	cct gat ttg aaa gat act ttc tgc agt agt ctc ctg ctc att tat aat ttt Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe 65 70 75 80	cct gat ttg aaa gat act ttc tgc agt agt ctc ctg ctc att tat aat ttt Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe 65 70 75 80
343	aag ata ttt gaa aga tat gga agc aga aac ttt gca tcc ttt tgc Arg Ile Phe Gln Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu 85 90 95	aag ata ttt gaa aga tat gga agc aga aac ttt gca tcc ttt tgc Arg Ile Phe Gln Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu 85 90 95
391	ctg ggt tcc tgg gtc ttc tgc gca gcc tta ttt gac ttc ctc att gaa Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Gln 100 105 110	ctg ggt tcc tgg gtc ttc tgc gca gcc tta ttt gac ttc ctc att gaa Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Gln 100 105 110
439	gct atg cag tat ttc ttc ggc atc acc gca gct agt aat ttc ctg cct tct Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser 115 120 125	gct atg cag tat ttc ttc ggc atc acc gca gct agt aat ttc ctg cct tct Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser 115 120 125
487	gga ttc ctg gca cct gtg ttt gct ctg ttt gta cca ttt tac tgc tcc Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser 130 135 140	gga ttc ctg gca cct gtg ttt gct ctg ttt gta cca ttt tac tgc tcc Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser 130 135 140
535	ata cca aga gtc caa gtc gca caa att ctc ggt ccg ttc tcc atc aca Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr 145 150 155 160	ata cca aga gtc caa gtc gca caa att ctc ggt ccg ttc tcc atc aca Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr 145 150 155 160
583	aac aag aca ttc att tat atc ttc gga ctc cag ctc ttc acc cct ggt Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly 165 170 175	aac aag aca ttc att tat atc ttc gga ctc cag ctc ttc acc cct ggt Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly 165 170 175
631	tcc tac atc ttc tgg att gta gcc ata agt gga ctc atg tcc ggt ctg tgc Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys 180 185 190	tcc tac atc ttc tgg att gta gcc ata agt gga ctc atg tcc ggt ctg tgc Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys 180 185 190

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	180	185	190	
	tac gac agc aaa atg ttc cag gtg cat cag gtg ctc tgc atc ccc agc	679		
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser			
	195	200	205	
5	tgg atg gca aaa ttc ttt tct tgg aca ctt gaa ccc atc ttc tct tct	727		
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser			
	210	215	220	
	toa gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac	775		
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp			
10	225	230	235	240
	atc cag aga cag cag aga atg gag ctg ctg gac cgg cag ctg atg ttc	823		
	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe			
	245	250	255	
	tct cag ttt gca caa ggg agg cga cag aga cag cag cag gga gga atg	871		
15	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Met			
	260	265	270	
	atc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta	919		
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val			
	275	280	285	
20	aac tat cag gcc ggt cgg cag tct gag cca gca gcg ccc cct cta gaa	967		
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu			
	290	295	300	
	gtt tct gag gaa cag gtc gcc cgg ctc atg gag atg gga ttt tcc aga	1015		
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg			
25	305	310	315	320
	ggg gat gct ttg gaa gcc ctg aga gct toa aac aat gac ctc aat gtc	1063		
	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val			
	325	330	335	
	gcc acc aac ttc ctg ctg cag cac tgatagtcac aggccaaacac tgg	1110		
30	Ala Thr Asn Phe Leu Leu Gln His			
	340			
	gacgggaacg gaagcagagt gacagtgagt ggtoaccacc atcagatcag cccgggggacc	1170		
	gagcactctet ggtgctgatg ttcttgtggg aagaggggagg ttccaccgca cccctgccct	1230		
	caaccgcgaag actgttgccg ttttagtggt gagataagtt tgccattaca ttgcatgta	1290		
35	ttttctatct atatttttta ttgggcattt tccctaggtt ggagagtacg caactogtttt	1350		





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	25	30	35	
	gaa gca gtg tgg acc gcg tac ctc aac gtg tcc tgg cgg gtt ccg cac			375
	Glu Ala Val Trp Thr Ala Tyr Leu Asn Val Ser Trp Arg Val Pro His			
	40	45	50	55
5	acg gga gtg aac cgt acg gtg tgg gag ctg agc gag gag ggc gtg tac			423
	Thr Gly Val Asn Arg Thr Val Trp Glu Leu Ser Glu Glu Gly Val Tyr			
	60	65	70	
	ggc cag gac tgg ccg ctg gag cct gtg gct ggg gtc ctg gta ccg ccc			471
	Gly Gln Asp Ser Pro Leu Glu Pro Val Ala Gly Val Leu Val Pro Pro			
10	75	80	85	
	gac ggg ccc ggg gcg ctt aac gcc tgt aac ccg cac acg aat ttc acg			519
	Asp Gly Pro Gly Ala Leu Asn Ala Cys Asn Pro His Thr Asn Phe Thr			
	90	95	100	
	gtg ccc acg gtt tgg gga agc acc gtg caa gtc tct tgg ttg gcc ctc			567
15	Val Pro Thr Val Trp Gly Ser Thr Val Gln Val Ser Trp Leu Ala Leu			
	105	110	115	
	atc caa cgc ggc ggg ggc tgc acc ttc gca gac aag atc cat ctg gct			615
	Ile Gln Arg Gly Gly Gly Cys Thr Phe Ala Asp Lys Ile His Leu Ala			
	120	125	130	135
20	tat gag aga ggg gcg tct gga gcc gtc atc ttt aac ttc ccc ggg acc			663
	Tyr Glu Arg Gly Ala Ser Gly Ala Val Ile Phe Asn Phe Pro Gly Thr			
	140	145	150	
	cgc aat gag gtc atc ccc atg tct cac ccg ggt gca gta gac att gtt			711
	Arg Asn Glu Val Ile Pro Met Ser His Pro Gly Ala Val Asp Ile Val			
25	155	160	165	
	gca atc atg atc ggc aat ctg aaa ggc aca aaa att ctg caa tct att			759
	Ala Ile Met Ile Gly Asn Leu Lys Gly Thr Lys Ile Leu Gln Ser Ile			
	170	175	180	
	caa aga ggc ata caa gtg aca atg gtc ata gaa gta ggg aaa aaa cat			807
30	Gln Arg Gly Ile Gln Val Thr Met Val Ile Glu Val Gly Lys Lys His			
	185	190	195	
	ggc cct tgg gtg aat cac tat tca att ttt ttc gtt tct gtg tcc ttt			855
	Gly Pro Trp Val Asn His Tyr Ser Ile Phe Phe Val Ser Val Ser Phe			
	200	205	210	215
35	ttt att att acg gcg gca act gtg ggc tat ttt atc ttt tat tct gct			903

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5	5	235	Arg Arg Leu Arg Asn Ala Gln Lys Arg Lys Gln Leu	240	245	Arg Arg Leu Arg Asn Ala Gln Lys Arg Lys Gln Leu	951
		220	225	230			
10	10	265	Lys Gln Gly Asp Lys Gln Ile Gly Pro Asp Gly Asp Ser Cys Ala Val	270	275		1047
		250	255	260			
15	15	280	Lys Ala Asp Ala Lys Lys Ala Ile Gly Arg Leu Gln Leu Thr Leu	290	295	Lys Ala Asp Ala Lys Lys Ala Ile Gly Arg Leu Gln Leu Thr Leu	1143
		310	305	310			
20	20	315	Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile	320	325	Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile	1191
		330	335	340			
25	25	345	Asn Gln Ile Ser Asn Ser Ala Ser Ser His Gln Asp Asn Arg Ser	350	355	Asn Gln Ile Ser Asn Ser Ala Ser Ser His Gln Asp Asn Arg Ser	1287
		360	365	370			
30	30	360	Gln Thr Ala Ser Ser Gly Tyr Ala Ser Val Gln Gly Thr Asp Gln Pro	375	380	Gln Thr Ala Ser Ser Gly Tyr Ala Ser Val Gln Gly Thr Asp Gln Pro	1335
		375	380	385			
35	35	380	Pro Leu Gln Ile His Val Gln Ser Thr Asn Gln Ser Leu Gln Leu Val	390	395	Pro Leu Gln Ile His Val Gln Ser Thr Asn Gln Ser Leu Gln Leu Val	1383
		395	400	405			
40	40	405	Asn His Gln Ala Asn Ser Val Ala Val Asp Val Ile Pro His Val Asp	410	415	Asn His Gln Ala Asn Ser Val Ala Val Asp Val Ile Pro His Val Asp	1431
		415	420	425			

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	aac cca acc ttt gaa gaa gac gaa act cct aat caa gag act gct gtt	1479
	Asn Pro Thr Phe Glu Glu Asp Glu Thr Pro Asn Gln Glu Thr Ala Val	
	410 415 420	
	cga gaa att aaa tct taanaatctgt gtaaatagaa aacttgaaacc attagt	1530
5	Arg Glu Ile Lys Ser	
	425	
	aataacagaa ctgccaatca gggcctagtt tctattaata aattggataa atttaataaa	1590
	ataagagtga tactgaaagt gctcagatga ctaatatattat gctatagtta aatggcttaa	1650
	aatatttaac ctgttaactt tttccacaa actcattata atatttttca taggcaagtt	1710
10	tctctcagtg agtgataaca acattttttag acattcnaaa ctgtcttcaa gaagtcacgt	1770
	ttttcattta taacaatttt cttataaaaa catgttgctt ttaaaatgtg gagtagctgt	1830
	aatcaccttta ttttatgata gtatcttaat gaaaaaact acttcttttag cttgggtgac	1890
	atgtgtcagg gtttttctcc aggtgcttat attgatctgg aattgtaatg taaaaagcaa	1950
	tgcaaaacta ggcgagtaact tcttgaaatg tctattttaag ctgctttaag ttaatagaaa	2010
15	agattaaagc aaatatattca tttttacttt ttctattttt taaaattagg ctgaatgtac	2070
	ttcatgtgat ttgtcaacca tagttttatca gagattatgg acttaattga ttggtatatt	2130
	agtgcacatca acttgacaca agattagaca aaaaattcct tacaaaaata ctgtgtaact	2190
	atttctcnaa cttgtgggat tttcnaaag ctacgtatat gaatcatcat actgtttgaa	2250
	attgctaattg acagagtaag taacactaat attggtcatt gatcttcgtt catgaattag	2310
20	tctacagaaa aaaaatgttc tgtaaaatta gtctgttgaa aatgttttcc aaacaatggt	2370
	actttgaaaa ttgagtttat gtttgaccta aatgggctaa aattatatta gataaactaa	2430
	aattctgtcc gtgtaactat aaattttgtg aatgcatttt cctgggtgtt gaaaaagaag	2490
	ggggggagaa ttccaggtgc cttaatataa agtttgaaag ttcatccacc aaagttaaat	2550
	agagctattt aaaaatgcac tttatttgta ctctgtgtgg cttttgtttt agaattttgt	2610
25	tcaaatata gcgaatttta ggcacaaaata aaacagacat gtattttgtt ttgctgaatg	2670
	gatgaacca ttgcattctt gtacactgat ttgaaatgtg gtaaatatgt cccaatttgt	2730
	attgattctc tttaaatata aaatgtaaat aaatatattcc aat	2773



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EE	Estonia						

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT, P 99/03929

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12N5/12 C07K14/705 C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED  
(Minimum documentation searched (classification system followed by classification symbols))

IPC 7 C12N C07K

Documentation searched other than the minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category<sup>1</sup> Citation of document, where appropriate, where appropriate, of the relevant passages

Relevant to claim No.

1-6	WO 98 21238 A (KATO SEISHI; PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) abstract 22 May 1998 (1998-05-22) page 17, last paragraph - page 18, paragraph 1	X
1-6	DATABASE EMBLEST6 [online] 22 July 1998 (1998-07-22), Accession Number A1057511, STRAUSBERG R: "H. sapiens cDNA clone IMAGE:1653181 3' similar to SM:YJK4 yeast P42929 hypothetical 16.2 kD protein in SMEI-MEF2 intergenic region" XP002123564 100% identity in 357 BP overlap with SEQ ID NO:11	X

Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

Special categories of cited documents:

- \* document defining the general state of the art which is not considered to be of particular relevance
- \* earlier document but published on or after the international filing date
- \* document which may have priority claims or priority claim(s) or which is cited to establish the publication date of another document
- \* document relating to an oral disclosure, use, exhibition or other means
- \* document published prior to the international filing date but later than the priority date determined

Date of the actual completion of the international search

23 November 1999

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

CUPIDO, M

## INTERNATIONAL SEARCH REPORT

 International Application No  
 PC JP 99/03929

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBLEST21 [Online] Accession Number AA 482452, 24 June 1997 (1997-06-24) HILLIER L ET AL.: "zv05b11.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 7527733 5'similar to SW:YJK4 yeast P42929 hypothetical 16.2 kD protein in SME1-MEF2 intergenic region" XP002123565 99.7% identity in 367 BP overlap with SEQ ID NO 11 ---	1-6
A	D'ANDREA ET AL: "Molecular Cloning of NKB1. A Natural Killer Cell Receptor for HLA -B Allotypes" JOURNAL OF IMMUNOLOGY, vol. 155, no. 5, 1 September 1995 (1995-09-01), pages 2306-2310 2310, XP002111500 ISSN: 0022-1767 abstract page 2307, right-hand column, line 16 ---	1-6
A	GILLEN C M ET AL: "Molecular cloning and functional expression of the K-Cl cotransporter from rabbit, rat, and human." JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 271, no. 27, 5 July 1996 (1996-07-05), pages 16237-16244, XP002119528 AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD., US ISSN: 0021-9258 abstract ---	1-6
A	KYTE J ET AL: "A SIMPLE METHOD FOR DISPLAYING THE HYDROPATHIC CHARACTER OF A PROTEIN" JOURNAL OF MOLECULAR BIOLOGY, vol. 157, no. 1, 5 May 1982 (1982-05-05), pages 105-132, XP000609692 ISSN: 0022-2836 cited in the application the whole document ---	1-6
P,X	DATABASE EMBLEST11 [Online] Accession Number AI 553893, 25 March 1999 (1999-03-25) STRAUSBERG R: "Homo sapiens cDNA clone IMAGE:2169115 3" XP002123566 100% identity in 375 BP overlap with SEQ ID 11 -----	1-6

# INTERNATIONAL SEARCH REPORT

In national application No

PCT/JP 99/03929

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1 ☐ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2 ☐ Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3 ☐ Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

see additional sheets

This International Searching Authority found multiple inventions in this International Application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6 partially

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest

☐ No protest accompanied the payment of additional search fees



FURTHER INFORMATION C NTINUED FROM PCT/ISA/ 210

1. Claims: Claims 1-6 partially

A protein comprising amino acid sequence SEQ ID NO 1, a DNA SEQ ID NO 11 or 21, encoding this protein, as well as an expression vector capable of expressing this sequence and a eukaryotic cell expressing the DNA

2. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 2 and DNA SEQ ID 12 and 22

3. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 3 and DNA SEQ ID 13 and 23

4. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 4 and DNA SEQ ID 14 and 24

5. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 5 and DNA SEQ ID 15 and 25

6. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 6 and DNA SEQ ID 16 and 36

7. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 7 and DNA SEQ ID 17 and 37

8. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 8 and DNA SEQ ID 18 and 38

9. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 9 and DNA SEQ ID 19 and 39

10. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 10 and  
DNA SEQ ID 20 and 30

11. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 31 and  
DNA SEQ ID 41 and 51

12. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 32 and  
DNA SEQ ID 42 and 52

13. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 33 and  
DNA SEQ ID 43 and 53

14. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 34 and  
DNA SEQ ID 44 and 54

15. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 35 and  
DNA SEQ ID 45 and 55

16. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 36 and  
DNA SEQ ID 46 and 56

17. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 37 and  
DNA SEQ ID 47 and 57

18. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 38 and  
DNA SEQ ID 48 and 58

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

19. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 39 and  
DNA SEQ ID 49 and 59

20. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 40 and  
DNA SEQ ID 50 and 60

21. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 61 and  
DNA SEQ ID 71 and 81

22. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 62 and  
DNA SEQ ID 72 and 82

23. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 63 and  
DNA SEQ ID 73 and 83

24. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 64 and  
DNA SEQ ID 74 and 84

25. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 65 and  
DNA SEQ ID 75 and 85

26. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 66 and  
DNA SEQ ID 76 and 86

27. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 67 and  
DNA SEQ ID 77 and 87

28. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 68 and  
DNA SEQ ID 78 and 88

29. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 69 and  
DNA SEQ ID 79 and 89

30. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 70 and  
DNA SEQ ID 80 and 90

31. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 91 and  
DNA SEQ ID 101 and 111

32. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 92 and  
DNA SEQ ID 102 and 112

33. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 93 and  
DNA SEQ ID 103 and 113

34. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 94 and  
DNA SEQ ID 104 and 114

35. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 95 and  
DNA SEQ ID 105 and 115

36. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 96 and  
DNA SEQ ID 106 and 116

37. Claims: 1-6 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Idem as subject 1 but limited to protein SEQ ID NO. 97 and  
DNA SEQ ID 107 and 117

38. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 98 and  
DNA SEQ ID 108 and 118

39. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 99 and  
DNA SEQ ID 109 and 119

40. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 100 and  
DNA SEQ ID 110 and 120

41. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 121 and  
DNA SEQ ID 131 and 141

42. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 122 and  
DNA SEQ ID 132 and 142

43. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 123 and  
DNA SEQ ID 133 and 143

44. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 124 and  
DNA SEQ ID 134 and 144

45. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 125 and  
DNA SEQ ID 135 and 145

46. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 126 and

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

DNA SEQ ID 136 and 146

47. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 127 and  
DNA SEQ ID 137 and 147

48. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 128 and  
DNA SEQ ID 138 and 148

49. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 129 and  
DNA SEQ ID 139 and 149

50. Claims: 1-6 partially

Idem as subject 1 but limited to protein SEQ ID NO. 130 and  
DNA SEQ ID 140 and 150

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PC JP 99/03929

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9821328 A	22-05-1998	AU 4885297 A EP 0941320 A	03-06-1998 15-09-1999
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